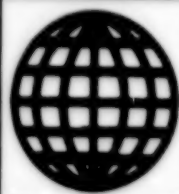


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# ***JPRS Report***

# **Science & Technology**

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***USSR: Life Sciences***

# Science & Technology

## USSR: Life Sciences

JPRS-ULS-91-001

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UDC 612.766.2-06:611.73-018.62

**Reactivity of Exhausted Human Skeletal Muscle  
Fibers Following Prolonged Antiorthostatic  
Hypokinesia**

907C0220 Leningrad ARKHIV ANATOMII,  
GISTOLOGIII I EMBRIOLOGII in Russian Vol 97  
No 7, Jul 89 (manuscript received 30 Sep 88) pp 53-59

[Article by S. L. Kuznetsov and V. V. Stepantsov,  
Institute of Biomedical Problems, USSR Ministry of  
Health, Moscow; First Moscow Medical Institute imeni  
I. M. Sechenov]

[Abstract] Ultrastructural and histochemical studies  
were conducted on skeletal muscle biopsies obtained  
from 8 men subjected to antiorthostatic hypokinesia for  
360 days, with and without exercise while in the ortho-  
static position. The data demonstrated that after 120 days

at a 6° antiorthostatic incline, there was extensive  
damage to the contractile and energetic element of the  
skeletal muscle fibers. Disorganization and destruction  
was seen to begin with the M-line and then to encompass  
the entire space between adjacent Z-lines. The Z-lines  
were unaffected, with the number of affected sarcomeres  
increasing with time. After 360 days, atrophic changes  
were particularly severe in the case of type I fibers.  
Metabolic deterioration was evident in diminished total  
protein and glycogen levels. Various forms of physical  
training in the antiorthostatic position were found to  
diminish the extent and progression of atrophy. The  
beneficial effects of physical exercise were directly pro-  
portional to the intensity of exercise and an early start of  
the exercise program. The relative stability of the  
cytoskeleton in the face of myosin and actin breakdown  
may explain the potential of the myofibrils for recovery.  
Figures 4; references 11: 5 Russian, 6 Western.

UDC 547.963.4:577.352.26

**Preparation of Liposomal Forms of Hemin Hydrophobic Derivatives**907C0245F Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript  
received 30 Dec 88) pp 1128-1132

[Article by I. P. Ushakova, G. A. Serebrennikova, Ye. A. Nikanorova, R. P. Yevstigeieva, Moscow Institute of Precision Chemical Technology imeni M. V. Lomonosov]

[Abstract] An erythrocyte model has been constructed on the basis of protoheme IX derivatives built into the liposome. This article describes the production of hemin lipid derivatives containing phosphatidylcholine, phosphatidyl ethanolamine and dihexadecyl glycerin groups, as well as covalently attached methyl histidine ester. The inclusion of the compounds synthesized in phospholipid vesicular membranes is studied. It is demonstrated that reduced forms of these systems have the ability to bind oxygen reversibly. Figures 1; References 14: 2 Russian, 12 Western.

UDC 577.175.82+612.82.015

**Rat Brain Tachykinin Receptors Bind  $\alpha$ -Bungarotoxin**907C0245C Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript  
received 30 Jan 89) pp 1030-1036

[Article by Yu. N. Utkin, Ye. M. Lazakovich, I. Ye. Kasheverov, S. F. Arkhipova, V. I. Tsetlin, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Tachykinins, along with the classical neurotransmitters, participate in nerve impulse conduction. There is interest in the mutual regulation of receptors of these two classes of transmitters. One of the tachykinins, substance P, influences the functioning of nicotinic acetylcholine receptors (ACR). Other similar tachykinins such as eledoisin are much less active. The influence of  $\alpha$ -bungarotoxin ( $\alpha$ -BT) and other neurotoxins on the binding of radioactive SP derivatives and eledoisin with rat brain membranes is studied to determine whether ACR ligands can bond with tachykinin receptors, particularly since information on the interaction of polypeptides other than tachykinins with these receptors is not available. It is found that  $\alpha$ -BT can effectively suppress bonding of labelled substance P and eledoisin derivatives with membrane and solubilized rat brain preparations. A number of other postsynaptic serpent neurotoxins also have less inhibiting activity. The data indicate that some of the  $\alpha$ -BT-binding brain peptides are tachykinin receptor components. Figures 3; References 37: 1 Russian, 36 Western.

UDC 577.112

**Argiopinin-Binding Protein from Bovine Cerebrum Membranes**907C0245B Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript  
received 30 Dec 88) pp 1022-1029

[Article by T. M. Bolkova, N. A. Avetisyan, T. G. Galkina, A. B. Kudelin, E. M. Makhmudova, M. M. Solovev, B. A. Tashmukhamodov, Ye. V. Grishin, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; Institute of Physiology, Uzbek Academy of Sciences, Tashkent]

[Abstract] A number of methods have been published for solubilization of glutamate-binding membrane components with ionic and nonionic detergents. This article undertakes solubilization of membrane preparations by means of sodium cholate, allowing the production of highly active argiopinin-binding protein preparations. A two-stage method was developed for subsequent purification of the receptor component, a combination of two affine chromatography steps using immobilized glutamate and argiopinins. The receptor preparations obtained had reproducible protein composition. The qualitative carbohydrate composition of the argiopinin-binding protein was also determined. The argiopinin-binding glycoprotein isolated in this work belongs to the membrane system of glutamate reception. Future studies of its reconstruction, cloning and expression, as well as its pharmacological characteristics, will determine its functional role in the neuronal conductivity of the mammalian brain. Figures 5; References 28: 7 Russian, 21 Western.

UDC 577.112.6:543.544

**High-Performance Liquid Chromatography of Peptide Bioregulators, Their Fragments and Derivatives. III. Sorption, Prediction of Retention Time and Peptide Analysis by Reversed-Phase HPLC**907C0245A Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript  
received 15 Sep 88; after revision 29 Dec 88)  
pp 1013-1018

[Article by V. D. Grigoryeva and V. D. Shatts, Institute of Organic Synthesis, Latvian Academy of Sciences, Riga]

[Abstract] A study is made of the specifics of chromatographic behavior and the prediction of retention time of unprotected linear and cyclical peptides. Models of retention time are compared for the octadecyl silica gels of two different manufacturers. Retention times were measured on 150 and 250 mm columns with inside



diameter 4.6 mm filled with Zorbax ODS, Silasorb C18 and Zorbax C8, particle size 5  $\mu$ m. Figures 2; References 6: 1 Russian, 5 Western.

UDC 577.151.042

**Synthesis, Structure and Anticholinesterase Activities of Methylthiophosphonate Derivatives of N-B-Oxyethylmorpholine and N-B-Oxypropylmorpholine**

907C0128A Tashkent KHIMIYA PRIRODNYKH SOYEDINENIY in Russian No 4, Jul-Aug 89 (manuscript received 10 Oct 88; in final form 30 Dec 88) pp 543-546

[Article by M. B. Gafurov, D. N. Dalimov, F. G. Kamayev, G. M. Vayzburg and A. A. Abduvakhobov, Institute of Bioorganic Chemistry imeni Acad. A. S. Sadykov, Uzbek SSR Academy of Sciences, Tashkent]

[Abstract] A series of methylthiophosphonates of N- $\beta$ -oxyethylmorpholine (I) and N- $\beta$ -oxypropylmorpholine (II) were synthesized, commencing with the condensation of morpholine with ethylene or propylene oxide in ethanol to prepare I and II, respectively. The final products, O-alkyl-O-[N-( $\beta$ -oxypropylmorpholinyl)]- and O-alkyl-O-[N-( $\beta$ -oxyethylmorpholinyl)] methylthiophosphonate were obtained, respectively, by the action of I and II on O-alkylmethylthiophosphonic acid anhydrides in triethylamine. Testing of the resultant compounds on acetylcholinesterase derived from human erythrocytes and equine serum butyrylcholinesterase showed that all behaved as mixed-type reversible inhibitors. The O-propyl analogs were generally more active by an order of magnitude than the other alkyl derivatives, while the butyl analogs differed in that they functioned as a noncompetitive reversible inhibitor. References 9: 7 Russian, 2 Western.

UDC 547.993

**Vasoactive Peptides from Venom of Wasp Polistes Gallicus: Isolation and Physicochemical and Functional Characteristics**

907C0128C Tashkent KHIMIYA PRIRODNYKH SOYEDINENIY in Russian No 4, Jul-Aug 89 (manuscript received 31 Aug 88; in final form 2 Jan 89) pp 564-568

[Article by V. M. Lvov, I. F. Mukhamedov and A. A. Akhunov, Institute of Bioorganic Chemistry imeni Acad. A. S. Sadykov, Uzbek SSR Academy of Sciences, Tashkent]

[Abstract] Conventional techniques of protein chemistry were utilized for the isolation of 6 vasoactive peptides from the venom of the wasp *Polistes gallicus*. Physicochemical analysis showed that their MW was approximately 1500  $\pm$  500 D, with a pI of around 10.5. Testing on smooth muscles revealed them to have a weaker

myotropic effect than bradykinin (BK). In terms of resistance to proteolytic digestion by a variety of enzymes (trypsin, chymotrypsin, carboxypeptidase), the following ranking was obtained: I > BK > II = VI > IV > V > III. Testing for hypotensive effects on cats following intravenous administration indicated that they were less potent than BK, but had an earlier onset and longer duration of action than BK. The data on duration of hypotensive action was in agreement with the data on susceptibility to proteolytic inactivation. Figures 1; references 10: 5 Russian, 5 Western.

UDC 547.96.07

**Synthesis of C-Terminal Fragments of Bombesin and of Their Analogs**

907C0128B Tashkent KHIMIYA PRIRODNYKH SOYEDINENIY in Russian No 4, Jul-Aug 89 (manuscript received 28 Jun 88; in final form 6 Jan 89) pp 554-564

[Article by I. L. Kuranova, S. I. Churkina, V. L. Lyudmirova, Ye. B. Filonova, F. M. Ibatullin, F. K. Mutulis, I. P. Sekatsis and V. D. Grigoryeva, Leningrad State University; Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Riga]

[Abstract] The carbodiimide and activated ester methods of peptide chemistry were employed for the synthesis of a series of analogs of the C-terminal end of bombesin. Biological testing of the peptides was conducted on rabbits, and involved assessment of the hypothermic effects following injection of 1  $\mu$ g of a preparation into a lateral ventricle of the brain at an ambient temperature of 10°C. The results demonstrated that only one product, [AcGln<sup>7</sup>]BN(7-14), possessed activity equivalent to bombesin. Preparations [DPhe<sup>7</sup>]BN(6-14) and [Pro<sup>6</sup>,Gly<sup>7</sup>,DAla<sup>11</sup>]BN(6-14) possessed only approximately 1 percent of the hypothermic activity of bombesin. Figures 5; references 13: 2 Russian, 11 Western.

UDC 577.112.083.3:519.68

**Determination of Amphipathic Structures in Protein Sequences**

907C0142F BIOORGANICHESKAYA KHIMIYA in Russian Vol 15 No 7, Jul 89 (manuscript received 14 Jul 88; in final form 25 Oct 88) pp 985-986

[Article by A. E. Gabrielyan, V. S. Ivanov and A. T. Kozhich, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] An analysis was conducted on amphipathic elements in the structure of epitopes of T-lymphocytes, based on a program that calculates paired correlation coefficients between hydrophobicity of amino acids and periodicity. Amino acid sequences with calculated correlation coefficients higher than the threshold value (0.6 for  $\alpha$  and  $3_{10}$  helices) were identified as possible

epitopes. Analysis of 90 sequences led to identification of 17 epitopes out of 22 known epitopes, whereas with the published AMPHI method a similar degree of identification required examination of 111 amino acid segments. The program used for the calculation can be run on an Apple IIe computer and is part of a utilities system designed for immunochemistry. References 6: 1 Russian, 5 Western.

UDC 635.21/24:[632.937.16+57.083.3]

#### **Detection of Potato X and M Viruses with Horseradish Peroxidase-Labeled DNA Probes**

907C0142E *BIOORGANICHESKAYA KHIMIYA*  
in Russian Vol 15 No 7, Jul 89 (manuscript received  
1 Sep 88; in final form 30 Jan 89) pp 947-951

[Article by Yu. F. Drygin, I. A. Afonina, K. Bayer, O. V. Nikolayeva and I. G. Atabekov, Interfaculty Special Problems Scientific Research Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy, Moscow State University imeni M. V. Lomonosov]

[Abstract] Trials were conducted on the detection of potato X and M viruses in extracts of infected potato tubers by means of blot-hybridization on nitrocellulose filters using horseradish peroxidase-labeled DNA probes. The DNA probes represented recombinant molecules obtained from phage M13 or single-stranded plasmid pTZ19 containing sequences complementary to the RNA of the viruses. The color reactions were developed with  $\alpha$ -chloronaphthol after hybridization. Although the enzyme-labeled probes were approximately 100-fold less sensitive than radiolabeled DNA probes, the system exhibited a sensitivity of 1 ng for the viruses, 30 pg for the purified viral RNA, and close to 50 pg for viral RNA in nucleic acid extract of potato tissue. Figures 3; references 15: 2 Russian, 13 Western.

UDC 577.113.6

#### **Using p-Nitrophenylethyl Blocking Groups in H-Phosphonate Synthesis of Oligodeoxyribonucleotides**

907C0142D *BIOORGANICHESKAYA KHIMIYA*  
in Russian Vol 15 No 7, Jul 89 (manuscript received  
11 Nov 88) pp 940-946

[Article by N. V. Skaptsova, A. N. Kurkin and A. V. Azhayev, All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] p-Nitrophenylethyl was demonstrated to function as an efficient blocking reagent of endocyclic amido groups of guanine and thymine nucleoside-3'-hydrophosphites in H-phosphonate synthesis of long oligodeoxyribonucleotide chains. Oligodeoxyribonucleotides 8-54 units long were readily synthesized by the combination of the fully blocked monomers with either

pivaloyl chloride (PivCl) or mesylenesulphonyl-3-nitro-1,2,4-triazole (MSNT). PivCl was found to be a more effective reagent than MSNT and was more stable on storage under argon. Nevertheless, both condensing reagents are suitable for manual synthesis of long oligodeoxyribonucleotides. Figures 3; references 23: 3 Russian, 20 Western.

UDC 577.112.6.083.3

#### **Synthesis and Immunochemical Characteristics of Peptide Sequences 59-72 and 25-36 of Human IL-2**

907C0142C *BIOORGANICHESKAYA KHIMIYA*  
in Russian Vol 15 No 7, Jul 89 (manuscript received  
18 Nov 88) pp 908-921

[Article by L. V. Onopriyenko, I. I. Mikhaleva, V. Ye. Lunev, V. A. Nesmeyanov and V. T. Ivanov, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Conventional wet chemistries were employed for the synthesis of amino acid sequences 59-72 and 25-36 of human interleukin-2 (IL-2), both of which sequences appear to represent antigenic determinants on the basis of previous immunochemical studies, calculations of secondary structure, and hydrophilicity profiles. Immunological studies led to the demonstration that both sequences function as antigenic determinants and elicited polyclonal rabbit antibodies when conjugated to KLH. The antibodies were active in solid phase ELISA. In addition, monoclonal antibodies against the 59-72 sequence were also obtained and confirmed in ELISA studies. The 59-72 antigenic determinant was shown to be a major epitope located in the C-end of IL-2 and may serve to generate antibodies that may be useful in isolating IL-2 produced by recombinant DNA technology. Figures 1; references 9: 2 Russian, 7 Western.

UDC 577.112.5:591.145.2-365

#### **Disulfide Bonds in Radianthus Macrodactylus Neurotoxin-III (RTX-III)**

907C0142B *BIOORGANICHESKAYA KHIMIYA*  
in Russian Vol 15 No 7, Jul 89 (manuscript received  
2 Nov 88) pp 904-907

[Article by T. A. Zykova and E. P. Kozlovskaya, Pacific Institute of Bioorganic Chemistry, Far Eastern Scientific Center, USSR Academy of Sciences, Vladivostok]

[Abstract] Conventional techniques of peptide analysis were used to identify the sites of disulfide bond in RTX-III isolated from the sea anemone *Radianthus macrodactylus*. Analysis of the peptide and fingerprints obtained with staphylococcal glutamine proteinase and trypsin showed that the following amino acid moieties are involved in S-S bond formation: Cys<sup>3</sup>-Cys<sup>43</sup>, Cys<sup>5</sup>-Cys<sup>33</sup>, and Cys<sup>26</sup>-Cys<sup>44</sup>. In view of the homology among

the various RTX toxins, it appears that they all shared identical positioning of the disulfide bonds. Figures 4; references 14: 4 Russian, 12 Western.

UDC 547.964.057+577.175.829'17.017

**Dermorphin: Synthesis and Structure-Activity Relationships of Analogs**

907C0142A *BIOORGANICHESKAYA KHIMIYA in Russian* Vol 15 No 7, Jul 89 (manuscript received 20 Jul 88) pp 869-903

[Article by G. A. Korshunova and N. V. Sumbatyan, Interfaculty Special Problems Scientific Research Laboratory imeni A. N. Belozerskiy and Chemical Faculty, Moscow State University imeni M. V. Lomonosov]

[Abstract] A survey of largely Western literature was conducted to summarize the structure-activity relationships of this unique opioid peptide (Tyr-D-Ala-Phe-Gly-Tyr-Pro-Ser-NH<sub>2</sub>), initially isolated in 1980 from the skin of the South American frog *Physomedusa*. The physiological spectrum of dermorphin activity has been shown to be due to the fact that it reacts with high affinity with  $\mu$  receptors and less efficiency with  $\delta$  receptors. Binding to  $\epsilon$  receptors is very weak, and interaction with  $\chi$  is negligible. Studies with longer, shorter, and substituent analogs demonstrated that Tyr<sup>1</sup>, Phe<sup>3</sup>, and Ser<sup>7</sup> are required for biological activity. D-Ala<sup>2</sup> protects the peptide from proteases; its replacement by D-Arg and D-Met-S-oxide enhance *in vivo* activity on systemic administration. Replacement of Tyr<sup>5</sup> by either L- and D- amino acids that have the same spatial size generally results in enhanced activity. Finally, Pro<sup>6</sup>

moiety imparts resistance to carboxypeptidase attack, while introduction of hydrophobic substituents into the C-terminus has been shown to increase bioactivity. References 121: 6 Russian, 115 Western.

UDC 547.962.02

**Theoretical Conformational Analysis of Litorin**

907C0120 *Minsk IZVESTIYA AKADEMII NAUK BELORUSSKOY SSR: SERIYA KHIMICHESKIKH NAUK in Russian* No 4, Jul-Aug 89 (manuscript received 6 May 88) pp 36-39

[Article by V. P. Golubovich, L. I. Kirnarskiy, Ye. N. Galyuk, V. V. Drboglav, I. N. Osipovich and A. A. Akhrem, Institute of Bioorganic Chemistry, Belorussian SSR Academy of Sciences]

[Abstract] Theoretical conformational analysis based on paired additive approximations was employed in further defining structural-functional parameters of litorin, a bioactive nonapeptide isolated from the skin of the Australian frog *Litoria aurea*. Litorin is a bombesin-like peptide differing from the former by the Phe<sup>8</sup> moiety rather than Leu<sup>8</sup>. The six most stable conformations ( $\Delta U$  at or below 10 kcal/mole) were found to represent highly compacted molecules of the following type: BBRRBH-BBB, BBRBBHBBB, RBRBBHBBB, RBRBBHBBB, BBRBBHBRB, and RBRBBHBRB. These preliminary findings may serve as a starting point for the design of conformationally restricted analogs, primarily [D-Ala<sup>6</sup>]-, [Pro<sup>5</sup>]-, and [Pro<sup>4</sup>-litorin. References 6: 3 Russian, 3 Western.

UDC 579.841.11.08

**Reutilization of Immobilized *Pseudomonas Putida* for Production of 2-Keto-D-Gluconic Acid***907C0214A Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 4, Jul-Aug 89 (manuscript received 10 Feb 87) pp 458-463*

[Article by K. A. Kravchenko, M. I. Voloshenko, Ye. N. Disler, S. A. Gulevskaya and G. K. Skryabin, Institute of Biochemistry and Physiology of Microorganisms, Pushchino, Moscow Oblast]

[Abstract] Trials were conducted with immobilized *Ps. putida* VKM-1301 cells used for the synthesis of 2-keto-D-gluconic acid (KGA) in order to improve on the productive half-life of 14 days. Periodic washing of the fibers with nutrient medium, pH 6.8-7.2, was found to extend the half-life to 48 days. Detailed examination of the preparation showed that this form of treatment resulted in creation of a mixed system of immobilized and free *Ps. putida* cells. However, after 48 days, despite ongoing treatment with the nutrient medium, production of KGA fell by a factor of 1.5 and remained at that level for the subsequent 34 days. Another sharp drop in KGA production occurred after 85 days, and by day 100 had bottomed out at 9-10 percent of the initial level. Thus, culture age was found to be the dominant factor determining production of KGA by *Ps. putida* immobilized on Ca-alginate. Finally, an interesting observation was that the older cultures of *Ps. putida* also produced 5-keto-D-gluconic acid in small quantities. Figures 2; references 9: 2 Russian, 7 Western.

UDC 543.545:579.018.52:578

**Purification of Bacterial and Viral Suspensions by Electropolarization on 'Segnetel' Adsorbent***907C0214B Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 4, Jul-Aug 89 (manuscript received 22 Aug 88) pp 479-484*

[Article by V. S. Andreyev, L. P. Gavryuchenkova, V. G. Popov, L. L. Sergeyeva, S. V. Timofeyev and L. N. Tsukanova, All-Union Scientific Research Institute of Highly Purified Biopreparations, Leningrad]

[Abstract] Efficiency of purification of bacterial and viral suspensions by electropolarization was tested on Segnetel, a composite adsorbent. Studies with suspensions of *E. coli* M-17 and *S. marcescens* B-1M10 cells in concentrations of  $10 \times 10^9$  to  $15 \times 10^9$  cells/ml, using elution with 0.85 percent NaCl, a potential of  $2 \times 10^3$  V and a 1.2 ampere current, showed efficient flow-polarization and electrodeposition. The degree of bacterial purification reached 90 percent after 4-5 cycles of operation, and 99 percent after 10 cycles. In addition, studies on purification of endonuclease from *S. marcescens* showed that a 100-fold reduction in cell concentration could be obtained after 9 cycles without

any loss of enzymatic activity. Trials with influenza A/Texas a/77 virus in chick allantoic fluid (35 V, 0.15 M phosphate buffer, pH 7.0; elution with 0.5 M tris buffer, pH 8.7, 1.0 M NaCl) yielded 30- to 40-fold better virus purification in terms of the protein concentration and a virus yield of 70-80 percent. These findings demonstrated that Segnetel is a suitable matrix for electrodeposition and flow-polarization columns with multiple cycles of operation. Figures 4; references 6: 4 Russian, 2 Western.

UDC 547.211

**Ethane Oxidation by Methane-Utilizing Bacteria***907C0214C Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 4, Jul-Aug 89 (manuscript received 23 Jan 87) pp 499-503*

[Article by A. G. Zhivotchenko, Ye. G. Davidova, Ye. S. Nikonova, M. N. Manakov and Ye. A. Gluskina, All-Union Scientific Research Institute of Biosynthesis of Protein Products, Moscow; Agricultural Academy imeni K. A. Timiryazev, Moscow; Moscow Institute of Chemical Technology imeni D. I. Mendeleyev]

[Abstract]  $^{14}\text{C}$  labeling was employed in studies designed to assess the kinetics of ethane oxidation by the methane-utilizing bacterium *M. capsulatus*. The kinetic studies, conducted at pH 6.2 and 42°C, resulted in the demonstration that ethane oxidation was predicated on the concentration of ethane, methane, and oxygen. The maximum rate of ethane oxidation was calculated at about 14 mM/g/h, exactly half the rate of methane oxidation—28 mM/g/h. Figures 5; references 14: 5 Russian, 9 Western.

UDC 579.096.83

**Computer-Controlled Fermenter for Microbial Cultivation***907C0214D Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 4, Jul-Aug 89 (manuscript received 12 Feb 87) pp 512-517*

[Article by K. Tiisma, T. Paalme and R. Vilu, Institute of Chemical and Biological Physics, Estonian SSR Academy of Sciences, Tallinn]

[Abstract] Schematic details and a cursory technical overview is presented of a computer-controlled fermenter assembly designed to optimized cultivation of microbial cells for biotechnological purposes. The system allows for monitoring and controlling growth and physiological status of the microbial biomass under a variety of specified conditions. The system is based on the the commercial Ultroferm-1601 fermenter (LKB, Sweden),  $\text{O}_2$ ,  $\text{CO}_2$ , and heat sensors (Leeds and Northrup, USA), an Apple-II computer, and an operational program written in BASIC. Constant optimization of several key parameters (pH, temperature, rate of



mixing, substrate utilization, etc.) within a narrow range offers maximum flexibility in the synthesis of target products. Figures 2; references 15 (Western).

UDC 577.175.722'14:152.34.042

**Effects of Synthetic Proteinase Inhibitors on Production of Recombinant Human Proinsulin Secreted by Genetically-Engineered *Bacillus Subtilis***

907C0142G BIOORGANICHESKAYA KHIMIYA  
in Russian Vol 13 No 7, Jul 89 (manuscript received  
9 Jan 89) pp 987-989

[Article by Ye. V. Parfenova, D. G. Popov, A. A. Novikov, V. E. Sterkin, A. Ya. Strongin, A. Yu. Aksinenko\*, O. V. Korenchenko\*, V. I. Fetisov\*, I. V. Martynov\* and V. B. Sokolov, All-Union Scientific Research Institute of Genetics and Breeding of Industrial Microorganisms, Moscow; \*Institute of Physiologically Active Substances, USSR Academy of Sciences, Chernogolovka, Moscow Oblast]

[Abstract] Two serine synthetic proteinase inhibitors were tested for their efficiency in limiting proteolysis of porcine insulin added to a *Bacillus subtilis* AK73 culture in L-broth over a 60-min period at 37°C. The incubate consisted of 10 ng/ml of insulin and 5  $\mu$ liters of 0.1 M of an inhibitor. The data showed that both agents inhibited degradation of insulin by the bacterial proteinases, with O,O-diethyl-1-(N- $\alpha$ -hydrohexafluoroisobutyl)amino-1-methylpropyl phosphonate (I) shown to be a more efficient inhibitor than O,O-diisobutyl-1-[2-(ethoxycarbonyl)aminoperfluoropro-2-yl]-1-methylpropyl phosphonate. Further studies demonstrated that addition of compound I to a concentration of 1 mM to a culture of *B. subtilis* AJ73 (pBINS1.0) genetically engineered to produce human proinsulin enhanced product yield. In control cultures production of proinsulin peaked at 7 h and thereafter fell rapidly. In the experimental cultures with compound I, maximum production was attained in 7 h and remained at the maximum level for the next 4 h as a result of inhibition of proteases in the culture medium. Figures 2; references 2 (Western).

UDC 663.18.002.5

**Technology of Microbial Synthesis Based on Combination of Dispersion and Separation**

907C0129A Moscow BIOTEKHNOLOGIYA in Russian  
Vol 5 No 3, May-Jun 89 (manuscript received 8 Jun 87)  
pp 277-284

[Article by V. G. Popov and Ya. Ya. Shpot, All-Union Scientific Research Institute of Biosynthesis of Protein Products; All-Union Scientific Research and Engineering Institute of Applied Biochemistry, Moscow]

[Abstract] Engineering factors that may be used for the optimization of microbial synthesis were analyzed with a view toward creation of a universal process applicable to a wide range of microorganisms. The fundamental problems concern preservation of homogeneity of the microbial cultures throughout bioreactor volume by means of turbulent pulses codimensional with cell size. A universally applicable process must be sufficiently flexible to accommodate various producing microorganisms and substrates. The entire process, from nutrient medium to concentration of the microbial product, can, in theory, be reduced to two fundamental operations: dispersion and separation. Consequently, design and engineering should concentrate on the creation of apparatus and technology with universal application in carrying out such operations. The basic design of the dispersion technology would appear to require improved rotor-blade mixing devices, while the requirement for separation would be best served by nonsedimenting centrifugal filtration. Two potentially useful schematics have been included to provide a starting point for implementation in microbial biotechnology, with the caveat that considerable difficulties may be anticipated in technology transfer from the laboratory to a plant setting. Figures 2; references 16: 7 Russian, 9 Western.

UDC 577.112.4

**Selective Adsorption of Individual Plasma Proteins on Silochromes**

907C0129B Moscow BIOTEKHNOLOGIYA in Russian  
Vol 5 No 3, May-Jun 89 (manuscript received  
29 Oct 86) pp 343-349

[Article by B. A. Shmatkov, V. V. Zuyevskiy, A. N. Turayev and I. P. Andrianova, Scientific Research Institute of Physicochemical Medicine, RSFSR Ministry of Health, Moscow]

[Abstract] Several grades of silochrome adsorbents were tested for their utility in selective adsorption of plasma proteins, using human hemoglobin and bovine serum albumin. Analysis of adsorption isotherms at room temperature in tris-HCl buffer, pH 7.4, showed that adsorption of both proteins followed the Langmuir adsorption equation. Silochrome capacity for both proteins approximated that of a monolayer system (2.5-2.6 mg/m<sup>2</sup>). The data demonstrated that differences in adsorption can be controlled by selecting silochromes with different pore diameters. The availability of silochromes in pore sizes ranging from 200 angstroms to 2000 angstroms indicates that adsorbents can be selected that show a high degree of selectivity for the various plasma proteins. Selectivity may also be enhanced through judicious choice of adsorption times and buffer systems. Figures 4; references 14: 13 Russian, 1 Western.



UDC 538.69:578.088

### High-Gradient Magnetic Separation of Cells Labelled with Magnetic Latex Particles. Part I. Precipitation of Labeled Cells

907C0129C Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 3, May-Jun 89 (manuscript received 5 Dec 86)pp 371-375

[Article by S. N. Podoynitsyn\*, V. N. Bakharev\*\*, Yu. V. Lukin, S. I. Turkin, I. A. Gritskova\*\*, V. P. Zubov and A. N. Buryakov\*\*, Institutes of Bioorganic Chemistry imeni M. M. Shemyakin and of \*Chemical Physics, USSR Academy of Medical Sciences, Moscow; \*\*Moscow Institute of Fine Chemical Technology imeni M. V. Lomonosov]

[Abstract] An improved technique was developed for magnetic separation of human erythrocytes and lymphocytes labelled with magnetic latex particles, using high-gradient magnetic separation on plate-type separators. The erythrocytes and Namalva line B lymphoblastoid cells were labelled by incubation with magnetic polystyrene or polyacrolein particles for 1 h at 22°C. The efficiency of cell deposition was found to be affected by cell concentration, flow rate, and the strength of the magnetic field. Better than 90 percent cell separation was obtained with labelled-cell concentrations of  $10^6$  to  $10^9$  cells/ml, a flow rate of  $0.66 \times 10^{-3}$  to  $1.33 \times 10^{-3}$  m/sec, and 0.5-0.75 T fields. In the absence of a field, only about 5 percent of the labeled cells were retained. In addition, with the plate-type separator, cell recovery was readily attained by washing the cells out of the separator with 10-12 ml physiologic saline. Figures 3; references 8: 3 Russian, 5 Western.

UDC 631.466.3

### Development of Production Lines for Industrial Microalgae Production and Processing

907C0129D Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 3, May-Jun 89 (manuscript received 29 Oct 86) pp 376-380

[Article by A. M. Karpov and O. N. Albitskaya, All-Union Scientific Research Institute of Biotechnology, Moscow]

[Abstract] A brief summary is presented of the advantages of industrial microalgae closed-systems as an environmentally safe branch of biotechnology. Several operations utilizing microalgae are described as processes that are cost-effective and pollution-free and yield a variety of products such as single-cell proteins, carbohydrates, free amino acids, vitamins, and lipid components. Open-system processes, on the other hand, have been plagued by technical difficulties, including contamination by other microorganisms and low productivity. Figures 1; references 16: 11 Russian, 5 Western.

UDC 663.1.002.5

### Interactive Procedures in Setting Up Industrial Microbiology Production Lines

907C0129F Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 3, May-Jun 89 (manuscript received 17 Dec 87)pp 384-389

[Article by B. G. Litvak, A. S. Ryvlin and A. B. Lidenzon, All-Union Scientific Research Institute of Biological Technology, Moscow]

[Abstract] A cursory outline is provided of an interactive procedure for enhancing the efficiency of industrial microbial processes. The basic approach is based on a system of algorithms designed to ensure optimization of a number of factors in the planning stages prior to plant construction. In the final analysis the interactive program is designed to provide acceptable alternative solutions as to equipment and operating conditions. Application of this method to yeast production at a hydrolysis plant demonstrated that a system of algorithms of the type covered in the article could lead to a reduction in the cost of yeast production by 7.95 rubles per ton and save the plant 490,000 rubles per year. References 5 (Russian).

UDC 578.851.86:083.34

### Time-Resolved Monoclonal Antibody Fluoroimmunoassay of Phytoviruses

907C0129G Moscow BIOTEKHNOLOGIYA in Russian Vol 5 No 3, May-Jun 89 (manuscript received 13 Jul 88)pp 390-399

[Article by M. Yu. Saarma, L. V. Yarvekyulg, Ye. G. Andreyeva and R. K. Siniyarv, Institute of Chemical and Biological Physics, Estonian SSR Academy of Sciences, Tallinn]

[Abstract] Time-resolved fluoroimmunoassays were applied to a series of potato viruses using specific monoclonal antibodies, in order to determine sensitivity of this method and its suitability for simultaneous determination of several viruses. The assays at hand involved labelling the antibodies with  $\text{Eu}^{+3}$ ,  $\text{Sm}^{+3}$ , or  $\text{Tb}^{+3}$ , lanthanides that have a narrow band of maximum fluorescence. Preliminary studies with potato leafroll virus yielded a sensitivity of better than 1 ng/ml, approximately a 100-fold improvement over the sensitivity of ELISA. In simultaneous assays, using antibodies labelled with different labels, the sensitivity for potato X and M viruses was on the order of 5 ng/ml, and for the leafroll virus, 100 ng/ml. Figures 5, references 29: 3 Russian, 26 Western.

UDC 577.112

**Advisability of Evaluating Mutagenicity of Interferon Inducers Based on dsRNA**

907C0129E Moscow BIOTEKHNOLOGIYA in Russian  
Vol 5 No 3, May-Jun 89 (manuscript received 4 Jan 87)  
pp 381-383

[Article by T. D. Dubatolova, A. B. Duzhak, A. N. Kostomakha, I. M. Levin, V. I. Masycheva and V. F. Podgornyy, Scientific Research Engineering Institute of Biologically Active Substances, Novosibirsk Oblast]

[Abstract] An analysis was conducted on the mutagenic potential of dsRNA isolated from *S. cerevisiae* M-437, one of the more established natural inducers of interferon. dsRNA was isolated by a conventional SDS detergent method [Diaz-Raiz, J., and Kaper, J., PREP. BIO-CHEM., 8 (1):1-17, 1978]. Bone marrow metaphase smears obtained from C57Bl/6 mice treated intraperitoneally with dsRNA preparations containing about 2 percent LiCl showed that 7.4-9.5 percent of the cells had chromosomal abnormalities, versus a control figure of 3.2-4.25 percent. Additional purification of the dsRNA to reduce the concentration of LiCl to 0.2-0.3 percent reduced the incidence of cells with chromosomal abnormalities to control baseline levels without an adverse impact on interferon production. Mouse trials demonstrated that LiCl was not mutagenic, suggesting the possibility that formation of dsRNA-LiCl complexes may be required for mutagenicity. These observations suggest the need for testing potential interferon inducers for mutagenicity and that isolation procedures should be modified to reduce LiCl to 0.3 percent or lower. References 12: 4 Russian, 8 Western.

UDC 663.18[577.112]

**Plasminogen Activator from Cell Line RH-PA**

907C0687A Moscow BIOTEKHNOLOGIYA in Russian  
No 3, May-Jun 90 (manuscript received 20 Nov 87)  
pp 10-13

[Article by V. A. Isachenkov, O. P. Vakulina, N. P. Nikolayeva, and N. V. Kravchenko, Institute of Biomedical Technology, USSR Ministry of Health, Moscow]

[Abstract] Continuous cell line RH-PA, derived from embryonic human kidney in 1961, was assessed as a source of plasminogen activator (PA). Enzyme-linked assay techniques based on rabbit antibodies against human urokinase led to the demonstration that cultivation in medium 199 resulted in the production of urokinase proenzyme in the proliferative phase of growth. After 4 days of culture, urokinase PA (uPA) showed an exponential increase, which was attributed to conversion of the proenzyme to uPA due to release of lysosomal trypsin-like enzymes as the culture began to degenerate. Conversion of the proenzyme to uPA was enhanced by addition of plasmin to the medium and inhibited by

addition of protease inhibitors. In addition, the activity of uPA was blocked by urokinase antibodies. These findings suggest that the RH-PA cell line may be viewed as a source of uPA. Figures 6; references 20: 6 Russian, 14 Western.

UDC 663.18

**Light-Dependent Formation of Ammonia by Immobilized and Free Cells of *Anabaena variabilis* Cyanobacterium Mutants**

907C0687B Moscow BIOTEKHNOLOGIYA in Russian  
No 3, May-Jun 90 (manuscript received 25 Nov 87)  
pp 18-22

[Article by Ye. Ye. Karyakina\*, V. B. Orozgozhoyeva\*\*, T. I. Struchalina\*\*, and S. D. Varfolomeyev\*, \*Moscow State University imeni M. V. Lomonosov; \*\*Institute of Organic Chemistry, Kirghiz SSR Academy of Sciences, Frunze]

[Abstract] Comparative studies were conducted on two mutant strains of *Anabaena variabilis* with derepressed nitrogenase in terms of light-induced (1000-10,000 lux; 28-32°C) formation and secretion of  $\text{NH}_4^+$ . Data on the mutants with repressed glutamine synthetase showed that mutant A. variabilis ED81 produced 43.0-48.0  $\mu\text{moles}$  of ammonia per 1 mg of chlorophyll-a per hour, while mutant ED92 produced 20.0-26.0  $\mu\text{moles/mg/h}$ . Maximum rate of ammonia production prevailed in the pre-exponential phase of growth. The rate of  $\text{NH}_4^+$  production diminished as the concentration reached  $5 \cdot 10^{-4}$  to  $10^{-3}$  M in the medium and the cultures entered logarithmic growth with metabolic assimilation of  $\text{NH}_4^+$ . The wild A. variabilis culture lacked a slow growth phase, which in the case of ED81 was approximately 10-12 days. Immobilization of the mutant cyanobacteria on fiberglass washed with acetone and pretreated with 30 percent aluminum chloride increased the productivity of ED81 and ED92 to 297 and 165  $\mu\text{moles/mg/h}$ , respectively, under conditions of intermittent operation. The yield of  $\text{NH}_4^+$  was diminished in continuous operation, a fact attributed to suboptimal bioreactor design. Accordingly, these observations suggest that A. variabilis ED81 and ED92 may be used for biotechnological production of  $\text{NH}_4^+$ . Figures 7; references 13: 7 Russian, 6 Western.

UDC 547.823

**Microbial Transformation of Nitrogen-Containing Heterocyclic Compounds. Part 1. Hydroxylation of Isomeric Methyl and Dimethyl Pyridines by Microscopic Fungi**

907C0687C Moscow BIOTEKHNOLOGIYA in Russian  
No 3, May-Jun 90 (manuscript received 14 Sep 89)  
pp 24-27

[Article by L. V. Modyanova, L. I. Vorobyeva, O. K. Shibilkina, Ye. V. Dovgilevich, P. B. Terentyev, and A.

N. Kost, Chemistry and Biology Faculties, Moscow State University imeni M. V. Lomonosov]

[Abstract] Microscopic fungi and one bacterium from a type culture collection were screened for their ability to transform nitrogen-containing heterocyclic compounds. The results demonstrated that the fungi *Beauveria bassiana* BKM F-2533 (ATCC7159), *Aspergillus sclerotiorum* JMJ 56673, *Asp. niger* NRRL 3228, *Tiegmella hyalospora*, *Absidia orchidis* 6, *Rhizopus nigricans* 7, *Trichotecium roseum* 27 and the bacteria *Pseudomonas fluorescens* transformed isomeric 2-, 3-, and 4-methylpyridines into the corresponding 2-, 3-, and 4-hydroxymethylpyridines. However, only *B. bassiana* produced preparative yields (42-45 percent) of pyridylcarbinol compounds. Studies with asymmetrical methylpyridines yielded the corresponding isomeric pyridylcarbinols. In all cases *B. bassiana* was the sole organism to produce the products in preparative yields. These findings suggest that microbial biotechnology may be utilized for the production of hydroxymethylpyridines as a one-step process carried out at room temperature, bypassing complex chemical synthesis requiring expensive reagents. References 19: 12 Russian, 7 Western.

UDC 663.18

#### Initial Phase of Animal Cell Cultivation on Microcarriers

907C0687D Moscow BIOTEKHNOLOGIYA in Russian No 3, May-Jun 90 (manuscript received 1 Feb 88) pp 58-62

[Article by A. A. Kudryavtsev, S. V. Smirnov, E. I. Lezhnev, and I. I. Popova, Institute of Biological Physics, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Kinetic studies were conducted on the adhesion of Chinese hamster fibroblasts to microcarriers to determine key parameters in the initial stages of the process. The adhesion experiments were performed with line B-11-d-ii-FAF-28, strain 431 cells in a mixture of Eagle's medium and medium 199 (1:1), supplemented with 10 percent bovine serum, at 37°C, pH 7.0-7.2. The microcarriers were represented by Tsitolat-1, a collagen product, with an average particle diameter of 230 µm, and a styrene-divinyl benzene (8 percent) copolymer (SDVBC) with an average particle diameter of approximately 200 µm. The adhesion plots showed that the time for 100 percent binding probability in the case of SDVBC was approximately 2.5 min, and for Tsitolat-1 was 1 min. In conjunction with total adhesion and distribution data, the results demonstrated that intervals between mixing should exceed 2.5 min for SDVBC and 1 min for Tsitolat-1 for uniform adhesion to occur. With greater intervals between mixing, the adhesive properties of individual cells cease to be a factor in binding, with net binding determined by the rate of cell sedimentation

and the intervals between mixing. However, if the intervals between mixing are too prolonged the fibroblasts tend to be distributed over the surface of a carrier unevenly. Figures 5; references 4: 2 Russian, 2 Western.

UDC 547.963.32

#### Construction of Family of Artificial Human Insulin Genes

907C0245D Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript received 10 Jan 89) pp 1070-1077

[Article by V. A. Yefimov, A. A. Buryakova, I. N. Pashkova, N. N. Polushin, O. G. Chakhmakhcheva, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Preproinsulin consists of a signal peptide, the A- and B-chains of insulin and a C-peptide. Preproinsulin is processed in the cell to proinsulin, then this inactive prohormone, as a result of proteolytic splitting of the C-peptide, is converted to insulin. This article describes the construction and cloning of a set of genes encoding human insulin, its biosynthetic precursors and their analogs. The methodologic approach is used to include oligonucleotide-directed mutagenesis and chemical-enzyme DNA synthesis. All structures produced were cloned in *E. coli* in the composition of plasmid vectors. The nucleotide sequences of the genes and corresponding amino-acid sequences of the structures are presented. Figures 5; References 14: 5 Russian, 9 Western.

UDC 577.217

#### Synthesis of Human Proinsulin in *Escherichia coli* Cells

907C0245E Moscow BIOORGANICHESKAYA KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript received 13 Feb 89; after revision 20 Mar 89) pp 1078-1090

[Article by V. A. Yefimov, I. V. Aleksyuk, A. A. Buryakova, I. N. Pashkova, N. P. Skiba, O. G. Chakhmakhcheva, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

[Abstract] Results are presented from studies of the expression of the human proinsulin gene in *E. coli* cells, the synthesis and cloning of which were described earlier by the same authors. Data are also presented on the isolation of this protein from the bacterial mass. Various vector systems are used, supporting both the direct expression of the prohormone and its synthesis as hybrid proteins. It is shown that proteolytic processing of the recombinant proinsulin forms human insulin. Figures 7; References 23: 6 Russian, 17 Western.

### Plague Outbreak in Guryev Oblast

907C0729A Moscow TRUD in Russian 27 Jun 90 p 2

[Article by V. Ilin: "We Are Reminded of the Plague. A Fatal Case in Guryev Oblast"]

[Text] On June 13, X., a twenty-seven-year-old transportation worker, developed a fever. On the same day he was placed into the railroad hospital at the Makat station, but on the sixth day he died. On June 21, the chilling results of tests made at the Guryev Anti-Plague Railroad Service were announced: A plague-causing culture had been isolated.

Information. The plague is a natural-focal disease that belongs to a group of particularly dangerous diseases. Of the three forms of the disease, bubonic, septic, and pulmonary, only the latter is spread by the air-droplet route, and is consequently capable of inducing an epidemic. The plague is transmitted to humans by fleas that usually live on rodents. The disease is cured by antibiotics best of all when detected in the early stage.

Approximately 10 percent of the territory of the Soviet Union—south of Rostov, Astrakhan, Arals, Barnaul, Irkutsk, and Ulan-Ude—constitute natural breeding grounds of the plague.

A TRUD correspondent asked Chief of the Plague Prevention Department of the Main Epidemiological Administration of the USSR Ministry of Health Yu. Fedorov to comment on the situation.

First of all let me say what has been done locally. In connection with the identification of the plague, two breeding grounds, as we call them have appeared. The first is at the residential site of the afflicted person, at the Zhaman-Sor station. A total of 370 persons reside there. An epidemiological investigation has shown that patient X. had primary contacts with ten persons. They have been placed under quarantine. The second focus is the railroad hospital at the Makat station where a quarantine has been established and 51 persons have been isolated. All the essential services have been put into action and a strict bacteriological control has been imposed. A high fever, which is the first sign of the disease, has not been exhibited by any of the persons placed under quarantine. If, as we hope, this will continue to be the case, then the quarantine will be lifted on June 27.

Disinfection and deratting, i.e., destruction of rodents, is underway in the village of Zhaman-Sor and along the railroad. Help, i.e., specialists and additional anti-epidemiological agents, has been sent to the foci.

[Correspondent] What form of the disease did N. have?

[Fedorov] The bubonic-septic type that is not transmitted through the air.

[Correspondent] But it could have also been the pulmonary type?

[Fedorov] Yes. Once this disease is in nature, there is always the danger that it will spread beyond the breeding focal zone. That is why the Ministry of Health has a special service in constant battle readiness. This consists of 29 local anti-plague stations and several zone institutes. They oversee endangered territories and when necessary, destroy rodents and undertake disinfection procedures.

[Correspondent] When did the world have the last plague epidemic?

[Fedorov] At the beginning of this century. Up to fifteen hundred cases are annually recorded in the world, most often in Africa. For example, an elevated morbidity rate has been observed in Madagascar for several months now. In our country the veil of secrecy regarding information about the plague was lifted two years ago. In 1988 there was one case, in 1989 there were two cases, one of which was fatal.

[Correspondent] I have been told that the danger of plague has been heightened, for example, by the construction of the Volga - Chogray canal...

[Fedorov] Yes, the construction of canals and railroads creates favorable conditions for the wider settlement of rodents in upturned earth.

[Correspondent] What should one do in order to avoid becoming ill?

[Fedorov] We give inoculations to the population residing in the natural breeding grounds. Inoculations are also given to students traveling to such sites as part of a construction detachment. But tourists, geologists, and other travelers should know that they should not put up camps in places where there are many burrows. If you come across a hare or fox that are easy to capture, be careful. They might be sick and therefore dangerous. Of course, the population should observe cleanliness at home. Constant training is being given to local medics on how to recognize plague symptoms and what should be done when they are detected.

[Correspondent] I was told in Astrakhan that the first secretary of the party obkom there, Vorodin, was extremely unhappy about the very fact that rodents exist in nature, and ordered the anti-plague station to destroy all of them to a head. It may be a laughing matter, but the question remains: If it is biologically impossible to catch all rodents and fleas, then will a guarantee that there will not be an epidemic be sufficient? After all, it is only two hours by plane from Guryev to Moscow...

[Fedorov] There can be no 100 percent guarantee in nature. But we can be confident that an epidemic will not occur. That is based on good training and concise work on the part of the anti-plague service, as is indicated by statistics.



**Statistics for Sexually Transmitted Diseases**

907C0729B Moscow *RABOCHAYA TRIBUNA*  
in Russian 15 Jul 90 p 3

[Article by F. Alekseyev: "An AIDS 'Competitor'?" ]

[Text] Even popular music groups are warning humankind: Have fear of AIDS. It is hard to believe that just 10 years ago no one would have even thought of a "twentieth century plague". There has been another "related" disease (at least with respect to the mode of transmission), and that is syphilis. How many people who are infected with syphilis do we have in our country?

Saratov

K. Mikhalev

We transmitted this question to the USSR Ministry of Health, and here is their reply:

According to official statistics there were 11,880 recorded cases of syphilis in the past year. The average per capita ratio was 4.1 cases per 1,000 inhabitants. According to estimates of specialists this figure corresponds to the incidence of syphilis in the 1960's. In addition, there were 226,322 recorded cases of another venereal disease, gonorrhea.

The USSR Ministry of Health has refuted rumors about the ostensible outbreak of domestic syphilis in Moscow.

The disease which was recently considered to be incurable is now being successfully controlled. Nevertheless, the consequences of syphilis are very severe. According to medical specialists, it remains a competitor to AIDS as a threat to humankind.

**Child Morbidity Statistics**

907C0729C Moscow *EKONOMIKA I ZHIZN'*  
in Russian No 29, Jul 90 p 16

[Statistical Report from the USSR State Committee for Statistics]

[Text]

**Child Morbidity for Infectious Diseases**

	Number of cases per 100,000 children under 15 years of age		
	1980	1985	1989
Influenza and acute upper respiratory tract infections	47,813	58,501	53,939
Chickenpox	2,051	2,301	2,111
Acute gastric infections, total	1,282	1,527	1,264
—including bacterial dysentery	396	541	337
Viral hepatitis	687	733	765
Scarlet fever	340	389	300
Mumps	1,473	657	206
Measles	494	336	57
Pertussis	21	76	49
Meningococcal infections	21	24	14
—including cerebrospinal meningitis	10	10	5

In 1989 there were also more than 3,000 pediatric cases of typhoid fever and paratyphoid fever, of which more than 2,000 cases (80 percent) were in the Central Asian republics, and there were 350,000 cases of rubella.

The number of therapeutic-prophylactic institutes according medical assistance to children is constantly growing. At the beginning of 1990 there were 18,000 polyclinics and divisions within those institutions. There were 87 hospital beds and 22 pediatricians per 10,000 children (under 14 years). Nonetheless, there were 190 work days lost in the national economy, computed per 100 working persons, as a result of the need to care for ill children (in 1985 there were 143 lost work days).



UDC 616.831-002-022:578.833.26]-036.21(571.61/.64)

**Tick-Borne Encephalitis in Northern Zone of Mixed Coniferous/Broadleaf Forests of Endemic Amur Region**

907C0211A Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 7, Jul 89 (manuscript received 6 May 88) pp 38-43

[Article by L. A. Vereta, O. V. Ostrovskaya, V. I. Volkov, N. M. Pukhovskaya, S. P. Nikolayeva, A. V. Shchukin, A. M. Dolgikh, V. I. Aleksandrov, T. V. Mzhelskaya, G. M. Voronkova, T. A. Zakharycheva and A. I. Skulkina, Khabarovsk Scientific Research Institute of Epidemiology and Microbiology, RSFSR Ministry of Health]

[Abstract] The Amur region represents the highest-risk area for tick-borne encephalitis (TBE) in the USSR, requiring special epidemiologic assessment of risk factors. In the northern reaches of the coniferous/broadleaf forests, the risk of TBE is especially high because of the virulence of the virus; mouse trials employing extra-neural injections showed that the TBE virus isolates frequently have titers in the range of 6 to  $>10$  log LD<sub>50</sub>, exceeding the titers seen in the southern zone. Analysis of morbidity and mortality patterns in the northern zone (Komsomol and Amur rayons) for 1963-1977 yielded respective figures of 112.92/100,000 and 16.3/100,000, which in the 1978-1987 period fell to 11.28/100,000 and 3.8/100,000. In the southern region (Khabarovsk and Vyazemskiy imeni Lazo rayons) the morbidity and mortality in 1963-1977 were 317.35/100,000 and 8.3/100,000, respectively, with corresponding figures of 47.65/100,000 and 5.2/100,000 in 1978-1987. The differences in the disease incidence and mortality in the two areas were attributed to intensive public health measures employed in the northern zone in connection with the construction of Baykal-Amur Railroad Line. References 9 (Russian).

UDC 616.831-002-022:578.833.26]-036-2(571.61/.64)

**Tick-Borne Encephalitis in Primorskiy Kray**

907C0211B Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 7, Jul 89 (manuscript received 9 Mar 88) pp 43-48

[Article by G. N. Leonova and G. P. Somov, Institute of Epidemiology and Microbiology, Siberian Branch, USSR Academy of Medical Sciences, Vladivostok]

[Abstract] An epidemiologic survey on the status of tick-borne encephalitis (TBE) in the Primorskiy Kray was conducted for the 1940-1987 timespan. In that period, there were 2,443 reported cases with a mortality of 20-25 percent. The morbidity pattern showed a progressive decline from an incidence of 4.87/100,000 in the 1940s to 2.92 in the 1960s to 1.7 in the 1980s, with considerable regional variation. The 31-40 age bracket generally had the highest incidence (7/100,000); 43.1 percent of the cases involved urban workers, 17.6 percent agricultural workers, 2 percent forestry workers, 5.8 percent preschool children, 17.5 percent school-age children, 9.8 percent retirees, and 3.9 percent other. Approximately 80 percent of the caseload was male. Virologic examination of 86,830 ticks revealed that the predominant vector was *Ixodes persulcatus*, followed by *D. silvarum*, *H. japonica*, *H. concinna*, and *H. longicornis*. The low rate of infectivity of the ticks evidently accounts for the small number of clinical cases and, hence, the low level of "herd" immunity in the local population. The Southern Okhotsk region of dark coniferous forests was confirmed to be a higher-risk area than the Eastern Asiatic region of mixed forests. In addition, in certain foci both TBE and Powassan virus were isolated. References 9 (Russian).

UDC 616.98:579.842.23]-036.22

**Sanitary-Epidemiologic Surveillance of Natural Plague Breeding Grounds**

907C0772A Moscow *VOYENNO-MEDITSINSKIY ZHURNAL* No 3, Mar 90 pp

[Article by Colonel of Medical Service A. P. Boroday, Lieutenant Colonel of Medical Service P. N. Arkhilov, Lieutenant Colonel of Medical Service K. G. Tolstov, and Candidate of Biological Sciences, Major of Medical Service A. I. Dubovoy]

[Abstract] The sanitary-epidemiologic surveillance of a natural breeding area for *Yersinia pestis* by means of epizootologic screening between mid-May 1988 and the end of June 1988 in two unnamed regions 60 km apart encompassed 1,157 rodents and 17,889 fleas found on them. Ten strains of *Y. pestis* were isolated from *Rhombomys opimus* great gerbils, fleas, and ticks. Twenty-two of the 1,157 sera samples had antibodies to *Y. pestis*, and over one-fourth of those testing positive were young animals, thus indicating that infection had been relatively recent. No pathologic alterations were noted in 75 percent of the incidences of *Y. pestis* in the animals, thus increasing the risk of plague infection.

UDC 616.932:616.9-098:575

**Inheritance and Expression of Cholera Toxin Genes Introduced Into *Vibrio cholerae* El Tor Cells Via Hybrid Plasmid**

907C0706A Moscow GENETIKA in Russian Vol 26  
No 2, Feb 90 (manuscript received 19 Dec 88)  
pp 206-214

[Article by N. I. Smirnova, G. A. Yeroshenko, L. F. Livanova, O. T. Mozharov, S. L. Filkova, and T. S. Ilyina, "Mikrob" All-Union Scientific Research Anti-plague Institute, Saratov; Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow]

[Abstract] An analysis was conducted on the inheritance and expression of cholera genes in recombinant plasmid pCO109 transferred into *Vibrio cholerae* RV79 by conjugation with *Escherichia coli* KS1685 (pCO109). pCO109 was constructed by cointegration of pOX38 (derivative of an F factor lacking IS elements) and pCT105 (derivative of pBR322 bearing cholera toxin operon vctA,B). Restriction studies demonstrated that in almost all cases pCO109 underwent dissociation in *V. cholerae* with loss of the pOX38 replicon and retention of pCT105; in *E. coli* K12 persisted in a stable state. This fact indicated that the F factor DNA cannot replicate in vibrio cells and that recombination between the two copies of the RS1 sequences of pCO109 is highly efficient in *V. cholerae* but not in *E. coli*. The cloned vctA,B genes, located on pCT105 as well as on the bacterial chromosome, were expressed in an efficient manner,

resulting in the synthesis of 3-5 µg/ml of cholera toxin. Figures 4; tables 1; references 16: 7 Russian, 9 Western.

UDC 579.252.5:579.841.31

**Identification of Symbiotic Plasmid of *Rhizobium phaseoli* 693**

907C0706B Moscow GENETIKA in Russian Vol 26  
No 2, Feb 90 (manuscript received 5 Dec 88) pp 215-221

[Article by T. V. Ivashina and K. M. Zlotnikov, Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Studies were conducted on the marking of cryptic plasmids of *Rhizobium phaseoli* 693 with transposon Tn5-Mob in order to identify a symbiotic plasmid bearing genes nod and nif. The cryptic plasmids were marked with the use of suicide plasmid pSUP5011, with the Mob sequence making possible mobilization of the marked plasmids in *Rhizobium phaseoli* and *Agrobacterium tumefaciens*. The studies revealed that nodulation genes in *Rhizobium phaseoli* 693 were located on plasmid pRP693b (approximately 190 MD). pRP693b and three other cryptic plasmids were nonconjugative and all bore, in addition to nod genes, melanin genes. The latter observation indicates that Mel<sup>+</sup> may be used as a marker for these plasmids, particularly since the nod and Mel genes appear to be in close proximity. Introduction of pRP693b into Nod<sup>-</sup> *R. phaseoli* strains and *A. tumefaciens* and expression of the nod gene in the recipients suggests that pRP693b may be used for improvement of agricultural bacteria. Figures 2; tables 1; references 17: 4 Russian, 13 Western.

UDC 615.33:578.245].03:[616.61-002.3-022:579.842.11].076.9

**Effect of Interferon on Experimental Colibacillary Pyelonephritis**

907C0636C Moscow ANTIBIOTIKI 1  
KHIMIOTERAPIYA in Russian Vol 35 No 1, Jan 90  
(manuscript received 26 Feb 88) pp 32-35

[Article by A. V. Rudenko, V. G. Maydannik, V. A. Pavlenko, N. Ya. Spivak, A. M. Romanenko, Ye. M. Ishchenko, L. P. Glebova, and Ye. N. Bavina, Scientific Research Institute of Urology and Nephrology, Ukrainian SSR Ministry of Health, Kiev]

[Abstract] Experimental therapeutic trials were conducted with interferon I in outbred mice to assess its efficacy in bacterial pyelonephritis. The experimental disease was induced in 12-14 g mice by injection of  $5 \cdot 10^7$  colibacillus cells into the right kidney, followed by 1000 U of interferon I on days 3 and 7. Comprehensive studies demonstrated that interferon I promoted rapid elimination of colibacillus from the kidneys and hindered invasion of the contralateral kidney. Histopathologic and gross observations demonstrated arrest of pathologic progression and attenuation of inflammation in the kidneys. In addition, phagocytic activity of neutrophils was enhanced in the interferon-treated animals, as was the percentage of thymic E-rosette forming cells. Tables 2; references 19: 14 Russian, 5 Western.

UDC 615.281:547.918].076.9

**Stimulation of Nonspecific Immunity Against Opportunistic Gram Negative Bacteria in Mice by Sea Cucumber Triterpene Glycosides**

907C0636B Moscow ANTIBIOTIKI 1  
KHIMIOTERAPIYA in Russian Vol 35 No 1, Jan 90  
(manuscript received 12 Aug 88) pp 23-26

[Article by A. M. Sedov, A. V. Apollonin, Ye. K. Sevastyanova, I. A. Alekseyeva, S. G. Batrakov, O. G. Sakan-delidze, V. G. Likhoded, V. A. Stonik, S. A. Avilov, and Ye. V. Kupera, Scientific Research Laboratory of Biologically Active Substances of Hydrobionts, USSR Ministry of Health, Moscow; Pacific Institute of Bioorganic Chemistry, Far Eastern Division, USSR Academy of Sciences, Vladivostok]

[Abstract] Experimental therapeutic trials were conducted with cucumarioside, a triterpene glycoside isolated from *Cucumaria japonica*, in outbred mice challenged with gram negative bacteria. Optimum benefit was obtained when cucumarioside was administered

intraperitoneally in a dose of 5 per 12-14 g mouse 3 days before an intraperitoneal injection of  $5LD_{50}$  dose of the bacteria. Whereas the mortality of untreated mice was 100 percent, cucumarioside improved the 21 day survival rate to 82.5 percent in *Pseudomonas mirabilis* challenged mice and to 40 percent in the *Escherichia coli* group. However, cucumarioside was ineffective against *Ps. aeruginosa*. In addition, cucumarioside was also shown to increase the  $LD_{50}$  dose for *Neisseria meningitidis* five-fold, and for *Salmonella minnesota* 4.3-fold. Consequently, cucumarioside was shown to enhance nonspecific immunity against certain Gram-negative bacteria. Failure of cucumarioside to protect against *P. aeruginosa* was attributed to rapid and overwhelming toxin production. Tables 3; references 14: 9 Russian, 5 Western.

UDC 615.339:578.245].015.4:612.128].07

**Activation of Interferon-Dependent Enzymes by Recombinant  $\alpha_2$ -Interferon in Patients with Chronic Hepatitis B**

907C0141 Moscow ANTIBIOTIKI 1  
KHIMIOTERAPIYA in Russian Vol 34 No 6, Jun 89  
(manuscript received 29 Sep 87) pp 472-475

[Article by T. M. Sokolova, N. P. Bugayeva, I. A. Suetina, F. I. Yershov and Ye. S. Ketiladze, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

[Abstract] An analysis was conducted on the serum levels of interferon and activities of 2',5'-oligoadenylate synthetase (OAS), histone kinase (HK), and aminotransferase (AT) in patients with chronic hepatitis treated with recombinant  $\alpha_2$ -interferon (reaferon; RAI). The study was based on a comparison of data obtained for donor controls, 10 patients prior to RAI treatment, and 16 patients treated with RAI for 1-3 months (1-3 million U, 2-3 times/week, i.m.). The results demonstrated that although OAS activity was depressed about fourfold in the untreated patients in comparison with donors, HK and interferon levels were equivalent in both groups. RAI treatment resulted in elevation of OAS to normal control level, HK rose to more than twice the control activity, as did the serum interferon concentration. Since OAS and HK mediate interferon activity, the data may be interpreted as reflecting therapeutic efficacy of RAI. In addition, serum AT fell significantly in 9 of 13 patients with elevated AT who were treated with RAI, providing additional confirmation of RAI effectiveness since AT serves as a viral marker. HBsAg levels and antibodies against the  $\delta$  agent were not affected. The RAI treatment scheme employed in this study was not optimal since it did not lead to a cure, despite improvement in blood chemistries. Figures 1; references 8: 3 Russian, 5 Western.

UDC 616.98:578.832.1]-092.9-085.361.438-036.8

### **Tactivin and Myelolipid Immunotherapy for Experimental Influenza**

907C0211D Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 7, Jul 89 (manuscript received 25 Mar 88) pp 89-92

[Article by N. N. Aleksandrova, V. Ya. Arion, A. V. Slobodenyuk and I. V. Sanina, Scientific Research Institute of Physicochemical Medicine, Moscow, and Sverdlovsk Scientific Research Institute of Viral Infections, RSFSR Ministry of Health]

[Abstract] Experimental studies were conducted on the effects of tactivin (T-activin) and myelolipid on influenza pathogenesis in BALB/c mice (10-12 g). The mice were challenged intranasally with 0.05 ml of a 100 LD<sub>50</sub> dose of influenza virus A/Texas/76 (H3N2) and subsequently treated either with tactivin (5 µg, s.c.), myelolipid (50 µg, s.c.), or a combination of both agents. Monitoring of the survival rates showed that all the control animals died within 15 days, whereas 100 percent survival after 21 days was obtained with the combined therapy administered on days 1 and 2 after the infection. Either agent alone was less effective, giving survival rates of 70-90 percent in the various trials. At no time could the virus be isolated from the lungs or thymus of mice on combined therapy, while either agent in isolation was less effective in inhibiting virus replication. Finally, the highest degree of MIF production was obtained with lymphocytes derived from mice treated with the tactivin + myelolipid combination, suggesting the need for clinical trials with this combination. References 12: 10 Russian, 2 Western.

UDC 615.275.4:612.112.94.015.2]-015.4.07

### **Preclinical Assessment of Human Interleukin-2 Pharmacodynamics**

907C0705D Moscow *PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA* in Russian No 2, Mar-Apr 90 (manuscript received 22 Mar 89) pp 32-34

[Article by N. V. Malakhova, I. D. Treshchalin, M. S. Iobadze, I. F. Abronina, S. N. Bykovskaya, S. F. Yushkov, E. R. Pereverzeva, A. B. Syrkin, and M. O. Raushenbakh, Laboratories of Cellular Immunity and Drug

Toxicology, All-Union Oncological Scientific Center, USSR Academy of Medical Sciences, Moscow]

[Abstract] A variety of preclinical trials with interleukin-2 (IL-2) demonstrated that IL-2 induced activation of killer cells exhibiting marked cytotoxic activities against human autologous and murine tumors. In addition, the survival rates of leukemia R 388-bearing mice treated with IL-2 was improved three-fold. The mouse studies also showed that IL-2 was relatively nontoxic, with changes such as thymic involution shown to be reversible upon discontinuation of IL-2. Additional studies on guinea pigs resulted in the loss of one animal to anaphylactic shock, which may have been due to a trace concentration of admixed human proteins. The generally greater clinical benefit of native human IL-2 over recombinant IL-2 preparation may be due to the presence of trace quantities of other lymphokines, as well as the fact that the N-terminal end of the native molecule is glycosylated. Tables 1; references 9: 4 Russian, 5 Western.

UDC 616.94-022.7:589.841.11]-084:615.371]-092.9

### **Experimental Studies on Preventive Inoculation on Pseudomonas Aeruginosa Sepsis in Burns**

907C0211C Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII* in Russian No 7, Jul 89 (manuscript received 25 Aug 88) pp 59-62

[Article by O. A. Bandman, Ye. S. Stanislavskiy, Ye. V. Kholodkova, T. V. Ivanova and V. F. Salov, Moscow Scientific Research Institute of Vaccines and Sera imeni I. I. Mechnikov, USSR Academy of Medical Sciences]

[Abstract] Experimental clinical trials were conducted on outbred and CBWA mice to assess the efficacy of a Pseudomonas aeruginosa protein vaccine [Stanislavskiy, E.S., et al., *VACCINE*, 3:128, 1985] in preventing sepsis in burns. Using intraperitoneal vaccination (0.1 mg protein 7 days before challenge) and a combination of intraperitoneal and subcutaneous (sublesion) challenge injections in control and experimental mice showed that the index of efficacy of the vaccine was > 3333.3. The LD<sub>50</sub> values in the experimental animals with burns on subcutaneous challenge was 30 bacterial cells, 5.1 x 10<sup>6</sup> cells in control animals with intraperitoneal challenge, and > 10<sup>5</sup> cells in the experimental mice. References 8: 2 Russian, 6 Western.



UDC 615.849.19.038:617.7

**Clinical Use of Novel Soviet Laser Device in Anterior and Posterior Chambers of Eye**

907C0774A Moscow VESTNIK OFTALMOLOGII in Russian Vol 106 No 3, May-Jun 90 (manuscript received 20 Apr 89) pp 22-23

[Article by A. V. Bolshunov, B. N. Malyshev, and D. M. Mashtakov, All-Union Scientific Research Center of Ocular Diseases, USSR Ministry of Health, Moscow]

[Abstract] Presented in this article are a technical description and the experimental results of a Soviet ophthalmologic device designed to coagulate and degrade ocular tissues. The two laser sources employed in the device are the YAG-laser (yttrium-aluminum-garnet) that operates continuously on a 0.532  $\mu\text{m}$  wavelength and a neodymium glass laser that operates at a 1.06  $\mu\text{m}$  wavelength in single and multiple modes. The potential use of this laser device in the treatment of abnormalities in the anterior and posterior chambers of the eye was studied in 48 patients, with results indicating that this device may be used for coagulation and degradation of ocular tissues. Figures 5; tables 1; references 3 (Russian).

UDC 616.12-005.4-085.849.19-036.8

**Combined Helium-Neon Laser Therapy in Ischemic Heart Disease Patients**

907C0776A Moscow KARDIOLOGIYA in Russian Vol 30 No 3, Mar 90 (manuscript received 10 Nov 88) pp 24-28

[Article by I. M. Korochkin, A. V. Kartelishev, G. V. Babushkina, and G. M. Kapustina, Chair of Internal Diseases No. 4, Second Moscow Medical Institute imeni N. I. Pirogov]

[Abstract] The effectiveness of laser therapy and possible mechanisms of its therapeutic effect on ischemic heart disease were studied on 177 patients aged 30-80 years divided into two groups to study the individual effects of topical (Group A) and intravenous (combined) (Group B) helium-neon laser (HNL) irradiation. Patients in Group A were treated in a manner as described in previous works (I. M. Korochkin, G. R. Romanova, et al., SOV. MED., No 2, 1984, pp 6-10, and I. M. Korochkin, A. V. Kartelishev, et al., SOV. MED., No 1, 1988, pp 23-27), while patients in Group B received a combined course of laser therapy with HNL irradiation consisting of two to six daily treatments, 1.5 mW, 45 min per session. Biochemical studies demonstrated a decrease in membrane-bound phospholipids with a concomitant rise in free cholesterol, thus indicating structural damage to the membranes. Stress tests were conducted before, immediately after, and 5 months after treatment. A 45 percent increase in the threshold capacity in functional class (FC) II and a 60 percent increase in FC III and IV patients indicate the beneficial effect of laser therapy. Combined HNL treatment was more effective than traditional treatment with figures of 89 and 84.5 percent versus a 55 percent remission for FC IV patients. Remission lasted 2-5 months in this group as compared to 5-7 months in FC II. An additional course of external laser therapy had the desired effect of extending the remission period. Intravenous laser therapy probably activates oxygen uptake, with catalase activating the enhancement of oxygen transport. The results demonstrated that low energy HNL irradiation acts indirectly on phospholipids and other lipids, and provides for structural organization with restoration of morphological and functional properties, including medicinal sensitivity. Figures 2; tables 1; references 8 (Russian).



### 'Stimulation' Medical Cooperative Uses Electrostimulation Therapy

907C0114 Moscow NEDELYA in Russian No 40, 2-8 Oct 89 p 7

[Article by Vladimir Starchevskiy, under the rubric "Returning to What Was Printed": "Just When Will It Be Time to Remove the Stones From the Road? A Unique Method for Treating Urological Diseases Is Having Difficulty Making It Through"]

[Abstract] The methods of electric and ultrasonic stimulation in urology developed by Aleksandr R. Guskov at the Central Scientific Research Aviation Hospital in Moscow a decade ago have not received approval from 'official' medicine, despite the fact that hundreds of patients have already benefitted from the procedures. Although promises of objective clinical trials and support have been made, Guskov and his colleagues are generally regarded as little better than charlatans, and the instruments that they have designed, Intraton-1 and Intrafon-2, have met with skepticism. Nevertheless, a medical cooperative named "Stimulation" has been formed to offer these forms of treatment in the management of kidney stones and prostatitis, for example. An average course of treatment takes 15-30 days and costs 150 to 350 rubles, which is below the average cost at medical cooperatives. In addition, war veterans, including veterans of Afghanistan, receive a 50 percent discount. In order to attract highly qualified medical personnel and keep the operation going, attempts are now being made to expand the scope of services to ophthalmology to generate additional revenue because an additional 25 percent surcharge has been placed on the cooperative. There is also hope of establishing similar cooperatives in other cities, as well as a research institute dealing with stimulation of organs and tissues.

UDC 616.895.8-085.361.438:547.96]-036.8

### Thymic Peptide Thymalin in Management of Schizophrenics With Therapeutic Resistance

907C0775A Moscow ZHURNAL NEVROPATOLOGII I PSIKHIATRII IMENI S.S. KORSAKOVA in Russian Vol 90 No 3, Mar 90 (manuscript received 29 Mar 89) pp 100-103

[Article by N. V. Govorin and O. P. Stupina, Chitinskiy Medical Institute]

[Abstract] The efficacy of the thymic peptide thymalin [sic] in the management of schizophrenics with therapeutic resistance was investigated in 44 patients aged 18-52 years with varying types of schizophrenia. These patients presented with a high level of antithymic antibodies and antibodies to psychotropic agents in addition to pharmacogenic resistance resulting from long-term psychopharmacotherapeutic use. Patients with psychopharmacotherapeutic resistance were administered 30 mg of thymalin intramuscularly every other day for 3-4 weeks.

Improvement was noted by the third to fourth injection in some patients and peaked at 2-3 weeks. Eighty percent of the patients in the experimental group noted significant improvement, while two experienced a deterioration in condition. Thymalin was more effective in cases of secondary (pharmacogenic) therapeutic resistance. In pathologic therapeutic resistance, thymalin acted as a psychostimulant. Thymalin enhanced T-lymphocyte functional activity and elimination of immune deficiency problems while lowering antibrain antibodies in the blood sera. The results suggest that the clinical and immunological correlations in schizophrenics indicate the significance of immune disorders in the formation of resistance and the complex and varied nature of these disorders. Tables 1; references 24: 20 Russian, 4 Western.

UDC 616.98:578.828]-092:616.017.1-064-021.5-07

### Novel Approach to Studying HIV-Infection Pathogenesis

907C0766A Baku AZERBAYDZHANSKIY MEDITSKINSKIY ZHURNAL in Russian No 4, Apr 90 pp 7-13

[Article by A. G. Rakhmanova, V. A. Isakov, V. S. Omelchenko, and F. A. Farzaliyev, Chair of Infectious Diseases and AIDS Laboratory Diagnosis, Institute for the Advanced Training of Physicians imeni S. M. Kirov, Leningrad]

[Abstract] The blood sera of 14 human immunodeficiency virus (HIV) positive individuals were investigated using conventional methods in addition to laser-correlation spectroscopy (LCS) to study the distribution of macromolecular structures in the blood sera. LCS demonstrated that AIDS patients have a polymodal histogram curve marked by viremia and large virus-containing immune complexes as compared to the bimodal histogram curve found in healthy people. Individuals with AIDS-related complex have a histogram curve that differs from that of both AIDS patients and healthy people in that it is typified by atypical proteins joined to immune complexes, with no sign of the virus in a free state. The differences in the histograms indicate various phases of the pathogenesis of the infection process. Figures 3; references 23: 13 Russian, 10 Western.

UDC 616.7-08:615.2:617.723

### Emoxypine Efficacy in Comprehensive Treatment of Ocular Diseases

907C0766B Baku AZERBAYDZHANSKIY MEDITSKINSKIY ZHURNAL in Russian No 4, Apr 90 pp 59-62

[Article by D. T. Gyulaliyeva, Ophthalmologic Hospital, Baku]

[Abstract] Emoxypine in a 1 percent solution was employed to treat 387 patients ranging in age from 16 to

60+ with various ocular diseases. The patients were divided into four groups. Group 1 consisted of those with vascular pathology (thromboses, and hemorrhaging resulting from hypertension, atherosclerosis, and diabetes). Conventional treatment with anticoagulants, antispasmodics, vasodilators, and vitamins was employed in addition to an emoxypine solution administered subconjunctivally or intramuscularly. Patients underwent treatment twice a year. Improvement was noted in all cases, with 50 percent of patients reporting good eye function. Group 2 consisted of patients with chorioretinal dystrophy and abiotrophy. Management consisted of comprehensive conventional treatment in addition to emoxypine injection. The twice yearly treatment resulted in

improved visual acuity in 62 percent of patients and stabilization in 38 percent. In the third group were patients who sustained eye injuries caused by a blunt instrument and marked by hemorrhaging. Vision was fully restored in 97.6 percent of this group employing only the emoxypine solution. Group four consisted of patients who had already been treated surgically. Subconjunctival emoxypine administration resulted in full visual restoration in this group. There were no apparent side effects from this treatment, nor was there any recurrence of hemorrhaging noted. Emoxypine is recommended not only for ocular pathologies, but also shows promise for use in vascular conditions and neurological and therapeutic practice.

UDC 579.843.95.083.33

**Dot-ELISA for Pestis F-1 Antigen***907C0132 Moscow LABORATORNOYE DELO in Russian No 6, Jun 89 pp 65-66*

[Article by T. A. Polunina, S. A. Korovkin and A. V. Naumov, "Mikrob" All-Union Scientific Research Institute, Saratov]

[Abstract] Studies were conducted on the design of a dot-ELISA for the determination of the F-1 antigen of *Yersinia pestis*, in analogy to the reported development of a dot-ELISA for cholera toxin [Beutin, L., et al., J. CLIN. MICROBIOL., 19(3):371, 1984]. Technical details included the use of rabbit IgG antibodies, Millipore nitrocellulose filters with 0.22-0.45  $\mu$ m pore diameters, and incubation in 0.01 M K-phosphate buffer, 7.4. Comparison of the results obtained with dot-ELISA, conventional EIA, and passive hemagglutination yielded respective sensitivities of 3.2, 19, and 25 ng/ml for the F-1 antigen. References 7: 4 Russian, 3 Western.

UDC 579.68

**Hydrocarbon Oxidizing Microorganisms of Arctic Waters and Ice**

*907C0208B Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 4, Jul-Aug 89 (manuscript received 18 Jun 87) pp 581-587*

[Article by T. V. Koronelli, V. V. Ilyinskiy, S. G. Dermicheva, T. I. Komarova, A. N. Belyayeva, Z. O. Filipova and B. V. Rozynov, Biological Faculty, Moscow State University imeni M. V. Lomonosov; Institute of Oceanology, USSR Academy of Sciences, Moscow]

[Abstract] Studies were performed on bacteria and yeasts isolated from Arctic ice and waters to assess their

capacity for growth on n-alkanes as the sole source of carbon and energy. The isolates consisted of 77 strains of bacteria (rhodococci, mycobacteria, arthrobacter, actinomyces) and 36 yeast strains. The bacterial isolates utilized the n-alkanes as the sole source of carbon and grew better at 18°C than at 4°C. The rhodococci and the saprophytic bacteria contained saturated and unsaturated C<sub>32-40</sub> mycolic acids, constituents lacking in the arthrobacter isolates. Further studies with rhodococci demonstrated their ability to degrade diesel fuel at 5-10°C and, more rapidly, at 26°C. In general, the bacteria utilized predominantly the C<sub>14-20</sub> n-alkanes and, to some extent, the higher MW components. C<sub>10-12</sub> n-alkanes and isoprenoids were utilized very slowly and may eventually be expected to accumulate in the Arctic environment, along with resins and petroleum asphalt. Figures 2; references 16: 12 Russian, 4 Western.

UDC 616.98:579.843.94]-078.73

**Magnetic Enzyme Immunoassay for Yersinia Pestis Antigens**

*907C0211D Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 89 (manuscript received 16 Jun 88) pp 62-66*

[Article by I. M. Klimova, V. I. Yefremenko and V. G. Pushkar, Volgograd Scientific Research Institute Antiplague Institute]

[Abstract] Conventional solid-phase EIA technology was modified for *Yersinia pestis* studies by the introduction of magnetic separation of the bound and unbound fractions. The magnetic solid phase consisted of magnetized polyacrylamide microgranules prepared by the method of V. G. Pushkar et al., [ZHURN. MIKROBIOL., No 12:30, 1985]. Analysis of standard curves showed that the sensitivity of the magnetic EIA in work with intact cells was 10<sup>4</sup> to 10<sup>5</sup> *Y. pestis* cells/ml, and 1-10 ng/ml in assays of the F-1 antigen. Figures 2; references 18: 9 Russian, 9 Western.

UDC 615.281:[547.976+547.673.1].074

**Studies of Condensed Complexes Formed by Linear and Circular Supercoiled DNA With Mitoxantrone and Bisantrone**

907C0636A Moscow ANTIBIOTIKI I  
KHIMIOTERAPIYA in Russian Vol 35 No 1, Jan 90  
(manuscript received 30 Dec 88) pp 19-22

[Article by V. I. Salyanov, Yu. M. Yevdokimov, and M. Palumbo, Institute of Molecular Biology, USSR Academy of Sciences, Moscow; University of Padua, Italy]

[Abstract] In order to better understand the mechanism of action of selected anthracenes and anthraquinones, circular dichroism (CD) analysis was conducted on the complexes formed by linear and circular supercoiled DNA (pBR322) with mitoxantrone (1,4-bis(6-hydroxy-1,4-diazoheptyl)-5,8-dihydroxy-9,10-anthracenedione dihydrochloride), an anthraquinone agent, and bisantrone (9,10-anthracenedicarboxaldehyde bis[(4,5-dihydro-1H-imidazol-2-yl)hydrazone] dihydrochloride), an anthracene. Evaluation of the spectra showed that amplitudes of the bands obtained with complexes involving circular supercoiled DNA were smaller than those with complexes formed by linear DNA. In contrast to linear DNA, filling of intercalation sites in supercoiled DNA by the chemical agents was accompanied by a change in the direction of the coil as evident in sign reversal of  $\Delta A$  on the CD spectrum and diminished electrophoretic mobility. Accordingly, the

data demonstrated that the intercalating agents exerted different actions on linear and supercoiled DNA molecules. Figures 5; tables 1; references 10: 4 Russian, 6 Western.

UDC 577.21

**Production of Unidirectional Deletions in Plasmid by Means of DNA 'Protector' and *Bal31* Exonuclease**

907C0245G Moscow BIOORGANICHESKAYA  
KHIMIYA in Russian Vol 15 No 8, Aug 89 (Manuscript received 29 Jul 88; after revision 27 Feb 89)  
pp 1137-1139

[Article by D. I. Nurminskiy, Yu. Ya. Shevelev, A. I. Kalmykova, Institute of Molecular Genetics, USSR Academy of Sciences, Moscow]

[Abstract] The achievement of a series of directed deletions beginning at the endonuclease recognition site in a DNA fragment is used in determination of the nucleotide sequence of extended DNA sections, and also in various gene engineering manipulations. Achievement of unidirectional deletions in a desired direction is frequently difficult. A convenient method for achievement of unidirectional deletions is suggested, based on the use of the exonuclease *Bal31* which hydrolyzes both chains of DNA in both directions from the restriction site, while protecting the portion of the plasmid desired by placing a fragment of DNA adjacent to it to act as a DNA protector. Figures 2; References 5; Western.

UDC 612.821.6

**Effects of Millimeter Wave Radiation on Conditioned Reflexes in Rats**

907C0701C Moscow ZHURNAL VYSSHEY  
NERVNOY DEYATELNOSTI IMENI I. P. PAVLOVA  
in Russia : Vol 40 No 2, Mar-Apr 90 (manuscript  
received 23 Aug 89; after revision 10 Jan 90) pp 377-379

[Article by S. V. Khromova and M. A. Kulikov, Institute  
of Higher Nervous Activity and Neurophysiology, USSR  
Academy of Sciences, Moscow]

[Abstract] The effects of millimeter wave irradiation on conditioned reflex behavior were investigated on 180-230 g male rats trained to perform in a Y-maze test. After the conditioned response was established, selected groups of animals were subjected to irradiation of either the occipital area of the head or the left hip area with 7.1 mm wave with a power output of 6-8 mW/cm<sup>2</sup> for one hour per day for ten days. The results demonstrated that only irradiation of the occipital area alleviated the neurotic-like state of indecision resulting from changing the conditioned stimulus. The latter suggests that the impact of millimeter waves on the conditioned response may have been due to acceleration of neural processing in the species under investigation. Figures 2; references 5 (Russian).



UDC 615.477.66.017:615.73.52].099.07

### Specific Activity and Toxicity of Hemostatic Ferracryl Plaster

907C0241 Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 52 No 4, Jul-Aug 89 (manuscript received 26 Sep 88) pp 48-52

[Article by K. M. Reznikov, R. I. Kitayeva, V. V. Yekimov, L. V. Zaporozhko, V. I. Leonov, A. N. Korzenko, N. M. Parfenova, YE. I. Peleshenko, L. I. Trukhacheva and N. A. Shchetinkina, Chair of Pharmacology, Voronezh Medical Institute imeni N. N. Burdenko]

[Abstract] Experimental clinical trials were conducted with the hemostatic ferracryl plaster to assess its safety and therapeutic efficacy. In addition to hemostatic properties, ferracryl has also been shown to possess moderate topical analgesic effects and antimicrobial activity against Gram-positive and -negative bacteria. The studies conducted on rabbits and guinea pigs with various form of cutaneous wounds and lesions demonstrated that plaster containing 3.12 percent by weight ferracryl accelerated hemostasis by 31.6-46.5 percent. In addition, a variety of monitoring techniques demonstrated that prolonged exposure was without adverse effects in terms of reflex determinations, electrocardiograms, hematologic examinations, or histologic skin and internal organ evaluations. Equally significant was the finding that ferracryl was nonallergenic. References 14 (Russian).

UDC 577.151.17

### Biological Optimization of Steady-State Processes

907C0208A Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 4, Jul-Aug 89 (manuscript received 6 Sep 88) pp 514-521

[Article by L. A. Piruzyan, V. A. Dement'ev and V. A. Lomonosov, Institute of Chemical Physics, USSR Academy of Sciences, Moscow]

[Abstract] A theoretical approach is taken to the optimization of biological steady-state processes, in conjunction with pharmacokinetic and pharmacodynamic information, to provide a basis for drug design. The purpose is to create adequate mathematical models based on biological control systems and physiological and pathological interrelationships to provide objective criteria for drug selection vis-a-vis target organ or system. Once sufficient data has been collated, computer simulation may be used to optimize dosage and administration schemes and provide prognostic criteria for clinical trials. References 15: 13 Russian, 2 Western.

UDC 615.31:547.58].012.1.07

### Synthesis and Pharmacodynamics of 1-Alkyl-3,4-Tetramethylene- $\beta$ -Carbolines

907C0165A Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 23 No 6, Jun 89 (manuscript received 4 May 88) pp 675-678

[Article by I. V. Komissarov, V. I. Dulenko, A. T. Dolzhenko, Yu. A. Nikolyukin, A. V. Kibalnyy, L. Ya. Zinkovskaya and O. G. Obraztsova, Medical Institute imeni M. Gorkiy, Institute of Physicoorganic Chemistry and Carbon Chemistry, Ukrainian SSR Academy of Sciences, Donetsk]

[Abstract] 1-Alkyl-3,4-tetramethylene- $\beta$ -carbolines I and II (alkyl = CH<sub>3</sub> in I, C<sub>2</sub>H<sub>5</sub> in II) were synthesized from the ketone indolylcyclohexanone by acid-catalyzed heterocyclization and were subjected to pharmacodynamic assessment on outbred albino rats (220 g). Compound I was found to be a more potent anxiolytic than II in conflict experiments with water deprivation. The anxiolytic effects of I were completely abrogated by pretreatment with compound CGC8216, an antagonist of benzodiazepine. In addition, compound I potentiated the effects of exogenous GABA and, in analogy to GABA, increased hyperpolarization electrotonic potentials of the ventral roots and depolarization of primary afferents in spinal cord perfusion studies. As an anxiolytic, compound I was less effective than diazepam by an order of magnitude in terms of dosage. In addition, doses 2.5- to 18-fold greater than diazepam were required in I and II to affect motor and orienting/exploratory activities, and a dose 100-fold greater was required to potentiate hexenal-induced sleep. Unlike diazepam (antagonistic effects), compounds I and II potentiated the convulsive effects of pentylenetetrazole and themselves induced convulsions in high doses. These observations suggest, therefore, that the anxiolytic effects of I and II involve mechanisms other than binding to GABA receptors. References 14: 8 Russian, 6 western.

UDC 615.281.8:012.1.07

### Synthesis and Antiviral Activities of 2,7-Bis[alkoxycarbonylmethoxy]fluoren-9-ones (BACMF)

907C0165B Moscow KHIMIKO-FARMATSEVTICHESKIY ZHURNAL in Russian Vol 23 No 6, Jun 89 (manuscript received 20 Apr 88) pp 702-704

[Article by L. A. Litvinova, S. A. Lyakhov, N. A. Zhukova, S. A. Andronati, V. I. Musiyenko, O. G. Yasinskaya, I. A. Vinograd, M. M. Kozlovskiy and O. Ya. Pentsarskiy, Physicochemical Institute imeni A. V. Bogatskiy, Ukrainian SSR Academy of Sciences, Odessa; Scientific Research Institute of Experimental Medicine, Ukrainian SSR Ministry of Health, Lvov]

[Abstract] BACMFs were synthesized by the reaction 2,7-dioxyfluoren-9-ones with alkyl bromoacetates by boiling in dimethylformamide in the presence of potassium carbonate. The 11 compounds that were synthesized were found to be weakly toxic for mice ( $LD_{50} > 1000$  to  $> 3000$  mg/kg). Most of the agents were also active against influenza virus A2/Texas in chick embryo and tick-borne encephalitis virus (TBEV) in mice, and behaved as moderately effective interferon inducers. In the final analysis, the most promise was shown by 2,7-bis(butyloxycarbonylmethoxy)fluoren-9-one against the influenza virus and by 3,6-dichloro-2,7-bis(propoxycarbonylmethoxy)fluoren-9-one against TBEV. References 5: 4 Russian, 1 Western.

UDC 615.849.1.015.25:547.789.3].012.1.07

#### Synthesis and Radioprotective Activity of S-[2-Amino-2-Methylpropyl]Isothiourea (AMIU)

907C0165C Moscow

KHIMIKO-FARMATSEVTICHESKIY ZHURNAL  
in Russian Vol 23 No 6, Jun 89 (manuscript received  
1 Mar 88) pp 709-711

[Article by A. A. Mandrugun, A. A. Rodyunin, V. M. Fedoseyev, G. V. Dontsova, O. N. Rakhmanina and M. M. Konstantinova, Chemical Faculty, Moscow State University imeni M. V. Lomonosov; Institute of Developmental Biology imeni N. K. Koltsov, USSR Academy of Sciences]

[Abstract] S-[2-amino-2-methylpropyl]isothiourea (I) was synthesized by the reaction of 2-amino-2-methylpropanol-1 with sulfuric acid to give 2-amino-2-methylpropyl sulfate (II), with II then reacted with NaOH to obtain 2-dimethylaziridine (III). In the final sequence, III was reacted with thiourea to obtain I dihydrobromide. Trials with (CBA x C57Bl)F<sub>1</sub> showed that the  $LD_{50}$  for compound I on i.p. administration was 164 mg/kg, i.e., compound I is considerably more toxic than S-(2-aminoethyl)isothiourea (IV). In addition, compound I was also inferior to IV in terms of radioprotection against 9.5-10.4 Gy gamma radiation and 7.0 Gy x-radiation. References 7: 4 Russian, 3 Western.

UDC 615.281.03:[616.98:579.842.23

#### Therapeutic Efficacy of Quinolones against Y. Pestis

907C0125A Moscow ANTIBIOTIKI I

KHIMIOTERAPIYA in Russian Vol 34 No 7, Jul 89  
(manuscript received 30 Dec 89) pp 521-523

[Article by V. B. Kalininskiy, N. T. Vasilyev and S. M. Yudin, Scientific Research Institute of Microbiology, Kirov]

[Abstract] Susceptibility testing *in vitro* and therapeutic trials *in vivo* were conducted to assess the efficacy of 4-quinolone-3-carboxylate derivatives against Y. pestis. The tube dilution data demonstrated that oxolinic acid, norfloxacin, enoxacin, ofloxacin, and ciprofloxacin were active against the various strains of Y. pestis in concentrations of 0.04-0.125 µg/ml, whereas nalidixic acid required concentrations on the order of 4-8 µg/ml for a similar degree of inhibition. The agents were also found to be effective as prophylactic and therapeutic agents in outbred mice (17-20 g) challenged s.c. with a 1000  $LD_{50}$  dose of Y. pestis 1300 and, on a dose basis, were fourfold as effective as in albino mice. Interestingly, oxolinic acid was less effective than the other agents *in vivo* than *in vitro*. References 9: 2 Russian, 7 Western.

UDC

615.332:577.182.75].033+615.332:577.182.75].036.8

#### Glycopeptide Antibiotics: Pharmacokinetics and Antimicrobial Activities of Eremomycin, Vancomycin and Teichoplanin

907C0126B Moscow ANTIBIOTIKI I

KHIMIOTERAPIYA in Russian Vol 34 No 7, Jul 89  
(manuscript received 9 Oct 88) pp 523-526

[Article by S. T. Filippovyan, I. V. Malkova and L. Ye. Goldberg, All-Union Scientific Research Institute for Screening for Novel Antibiotics, USSR Academy of Medical Sciences, Moscow]

[Abstract] Pharmacokinetic assessment was conducted on eremomycin, vancomycin and teichoplanin on white male rats (100-120 g) via subcutaneous and intravenous administrations of 50 mg/kg of the agent being investigated (vancomycin studies involved only intravenous administration). Evaluation of the various pharmacokinetic parameters showed that AUC values for eremomycin, teichoplanin, and vancomycin were 186.9, 412.4, and 62.1 (µg x h)/ml, respectively. The  $Cl_T$  values were 0.445, 0.202, and 1.34 ml/min for the respective compounds, and the corresponding MRTs were 4.9, 5.3, and 3.1 h. In addition, tube dilution studies with 50 methicillin-resistant strains of golden staphylococcus demonstrated that eremomycin was four times as effective as the other two agents. Finally, the bioavailability of eremomycin and teichoplanin was calculated at 94 percent with both routes of administration on the basis of the AUC data. Figures 1; references 5 (Russian).

UDC 615.334.015.2:615.275].015.4:612.017.1].07

**Multifactorial Analysis of Indicators of Immunity Following Combined Use of Doxycycline and Low MW Microbial Immunomodulators**

907C0126C Moscow ANTIBIOTIKI I  
KHIMIOTERAPIYA in Russian Vol 34 No 7, Jul 89  
(manuscript received 11 Oct 88) pp 526-530

[Article by A. V. Nikitin, I. P. Fomina, L. P. Ivanitskaya, V. M. Fishman and L. Ye. Bodunkova, All-Union Scientific Research Institute of Antibiotics, Moscow]

[Abstract] Multifactorial analysis was conducted on antibody response and development of delayed hypersensitivity (DH) to a fraction of *Y. pestis* EV vaccine as modulated by combined administration of doxycycline and a low MW microbial immunomodulator. The latter, designated M1, had been isolated from soil bacteria. The mathematical analysis and constructed nomograms demonstrated that the combination of the antibiotic with M1 leads to a certain degree of dissociation of the humoral response and DH. In general, the combination compensated to some extent the inhibition of DH seen with high doses of the antibiotic, and it restored a full humoral response with high doses of the antibiotic when M1 was administered after immunization. This approach, then, facilitates relative assessment of the effects of various factors on different pathways of the immune response and may be used in devising optimum therapeutic schemes of administration and dosage. Figures 3, references 2 (Russian).

UDC 615.22:547.898].076.9

**Effects of 12-Crown-4 and 15-Crown-5 on Cardio- and Hemodynamics**

907C0771A Moscow  
KHIMIKO-FARMATSEVTICHESKIY ZHURNAL  
in Russian Vol 24 No 3, Mar 90 (manuscript received 20 Dec 88) pp 29-31

[Article by K. G. Gurbanov, G. V. Kovalev, N. V. Seredintseva, and O. V. Ivanov]

[Abstract] The effects of crown esters 12-crown-4 and 15-crown-5 on cardio- and hemodynamics were evaluated to assess their potential as cardiovascular agents in experiments performed on 2.5-3.5 kg cats. In the first series of experiments the cats were administered 20 mg/kg of the substances to analyze the dose-dependent effects. In the second series of experiments, the effects of the substances on the cardiovascular system following administration of 10 mg/kg of the substances were recorded. The 12-crown-4 substance had no effect on the cardiovascular system, while the 15-crown-5 substance affected arterial pressure, left ventricle contraction, heart rate, and other parameters. The most probable explanation for these observations is that the crown esters form complexes with sodium ions on cell membranes, thus inhibiting sodium-potassium metabolism and causing hypotension and negative inotropic and negative chronotropic effects. These data provide the grounds for searching for peripheral vasodilators among crown ester derivatives. Figures 1; tables 1; references 10: 7 Russian, 3 Western.

UDC 612.886.9-06:613.16

**Gravitation Receptor Reaction in Response to Effect of Acceleration**

907C0669 Kiev *ZHURNAL USHNYKH. NOSOVYKH I GORLOVYKH BOLEZNEY* in Russian No 2, Mar-Apr 90 pp 8-13

[Article by A. T. Pakunov; Chair of Otorhinolaryngology (head—professor A. A. Lantzov) and Morphology, Department of Central Scientific Institute of Leningrad (head—director of medical sciences V. F. Ivanov), Leningrad Sanitation and Hygiene Medical Institute]

[Abstract] A further study of gravitation receptor reaction involved reproduction of gravitational overloading with the use of a centrifuge with radius of rotation of 100 cm and 95 revolutions per minute. The force of centrifugal acceleration was 10.05 g and the duration of effect was 5 minutes. Experiments on 6 guinea pigs and 4 rabbits exposed to this acceleration showed a pronounced increase in gravitation reaction. All experimental animals remained motionless for the 1st 5 minutes after end of the effect of acceleration. Marked disturbance of coordination of movement was noted for at least 1 hour. Electron microscopy study of the gravity receptor (utricle) revealed rather pronounced disturbances in many structures: bulging of some of the pillar cells cytoplasm into the endolymphatic space, surrounding of cynocilia by cytoplasmic matrix, cytoplasm vacuolization, decrease of cell nuclei electron density and pronounced dilatation and clarification of calicous nerve terminals. The presence around the cynocilia of a matrix resembling cytoplasm indicated that bulging of part of the cytoplasm from the pillar cells prevents intense excitation of the receptors. It is possible that, after a 10-minute overload, the advantage of bulging of some of the cytoplasm from the pillar cells involves limitation of mobility of the cynocilia surrounded by the cytoplasmic matrix. Figures 4; references 12: 10 Russian; 2 Western.

UDC 617-001-036.17-085.835.3-036.8-07:616.1-008.1

**Effects of Hyperbaric Oxygenation on Central Hemodynamics and Oxygen Consumption in Severe Physical Trauma**

907C0705B Moscow *PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA* in Russian No 2, Mar-Apr 90 (manuscript received 19 Oct 88) pp 26-28

[Article by A. G. Magomedov, Voronezh Oblast Clinical Hospital]

[Abstract] Therapeutic trials were conducted with hyperbaric oxygenation on outbred 12-18 kg dogs subjected to a gunshot wound with skeletal damage. The animals were divided into groups on the basis of treatment and

subjected to central hemodynamic and ventilatory monitoring in conjunction with assessment of clinical chemistries. In general, severe trauma complicated by 20-25 percent hypovolemia led to 100 percent mortality of untreated dogs within 1 h 25 min to 3 h of the onset of shock. Animals managed in the conventional manner presented with a 29.4 percent survival rate. Finally, animals managed with hyperbaric oxygenation (1-2 atm pressure for 50 min; 4-5 sessions, for 3 days) in combination with conventional medical and surgical management had a survival rate of 76.2 percent. Hyperbaric oxygenation-managed dogs showed a rise in circulating blood volumes, cardiac index and  $\text{VO}_2$ , facilitating correction of all forms of oxygen deficiency. Figures 1; tables 1; references 5 (Russian).

UDC 615.31:[547.95:547.943].03:616.127-005.4].015.4.076.9

**Cardioprotective Effects and Mechanisms of Novel Soviet Synthetic Endogenous Opioid Analog in Total Myocardial Ischemia**

907C0705A Moscow *PATOLOGICHESKAYA FIZIOLOGIYA I EKSPERIMENTALNAYA TERAPIYA* in Russian No 2, Mar-Apr 90 (manuscript received 27 Apr 88) pp 13-16

[Article by G. F. Dvortsin, Institute of Surgery imeni A. V. Vishnevskiy, Moscow]

[Abstract] A series of perfusion studies were conducted with isolated heart preparations derived from 180-350 g male Wistar rats which demonstrated that a novel Soviet synthetic analog of endogenous opioids—Tyr-Pro-Ala—exerts a cardioprotective effect. Subjecting an isolated heart to total ischemia in physiologic solution at 37°C led to irreversible myocardial damage. However, perfusion with  $3 \times 10^{-9}$  M of the tripeptide for 10 min, followed by 30 min of total ischemia, was followed by recovery of 80-100 percent of functional activity. Additional studies with intramuscular (10 µg/kg) and intragastric (100 µg/kg) administration of Tyr-Pro-Ala 30 min before total ischemia also demonstrated increased myocardial tolerance to stress. Further studies on administration of the tripeptide with propranolol and atropine and in combination with calcium perfusion led to the conclusion that Tyr-Pro-Ala acts via adrenergic mechanisms and controls calcium effects on the heart. These observations suggest that Tyr-Pro-Ala may have applications in heart surgery. Figures 4; references 14: 4 Russian, 10 Western.

**Neuroinformatics: Basis, State of the Art, and Prospects**

907C0244C Moscow *FIZIOLOGIYA CHELOVEKA* in Russian Vol 15 No 4, Jul-Aug 89 (manuscript received 10 Nov 88) pp 130-149

[Article by Yu. D. Kropotov, Institute of Experimental Medicine, USSR Academy of Medical Sciences, Moscow]



[Abstract] Neuroinformatics represents a new trend in studies on the brain and mental processes. It was developed by the author under the aegis of Academician N. P. Bekhtereva at the Scientific Research Institute of Experimental Medicine, and it concentrates on the development of a body of knowledge dealing with neuronal information processing. Analysis of higher nervous function as information processing consisting of neural networks, with the circuitry modified by neuronal plasticity, entails combination and correlation of planned experiments, theory, and intuition based on psychological observations. Further advances in neuroinformatics will come from a detailed understanding of neuronal function in the various brain formations during information processing, as well as an understanding of the individual neuronal elements as components of organic and physiological systems. Such understanding can only be assured by theoretical insight based on information derived from sophisticated experiments and mathematical modeling. Figures 5; references 45: 29 Russian, 16 Western

UDC 612.821+159.9

#### Integral Indicator of Visual Information Processing

907C0244B Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 15 No 4, Jul-Aug 89 (manuscript received 31 Jan 88) pp 97-102

[Article by N. V. Makarenko and V. V. Kalnish, Institute of Physiology imeni A. D. Bogomolets, Ukrainian SSR Academy of Sciences; Scientific Research Institute of Labor Hygiene and Occupational Diseases, Ukrainian SSR Ministry of Health, Kiev]

[Abstract] Tachyscopic studies were conducted on 70 men, aged 19-23 and matched as closely as possible as to occupational and physiologic characteristics, in order to determine the feasibility of deriving an integral indicator of visual information processing. The study involved assessment of error rate in speed and accuracy of identification of visual signals addressed to the first or second signal system. Analysis of the distribution patterns revealed a pattern skewed toward slow responses and inaccuracy. The resultant data were used to devise integral indicators for speed and accuracy in visual information processing, based on linear discriminant functions [Loskutova, T.D., FIZIOL. ZHURN. SSSR, 61(1):1, 1975]. The coefficient of correlation between the two parameters was on the order of 0.62 ( $p < 0.001$ ), pointing to significant similarity in the mechanisms responsible for information processing at the level of the first and second signal systems. Figures 1; references 9 8 Russian, 1 Western.

UDC 591.1

#### Effects of Embryonal Brain Tissue Transplants on Reactivity to Brain Injury in Rats

907C0208C Moscow IZVESTIYA AKADEMII NAUK SSSR: SERIYA BIOLOGICHESKAYA in Russian No 4, Jul-Aug 89 (manuscript received 2 Jul 87) pp 605-609

[Article by Ye. V. Loseva, I. V. Yermakova and T. S. Mikheyeva, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow]

[Abstract] A histological study was conducted on the effects of embryonal brain homotopic implants in adult rats on the sequelae of brain injury in the latter. The experimental model consisted of outbred male rats with deep electrolytic, mechanical or combined amygdaloid injury. The implants, amygdaloid or occipital tissue, were derived from rat embryos 18-21 days old. Histologic monitoring of the outcome over a 1.5-month period demonstrated unequivocally that the embryonal implants aborted the onset of autoimmune inflammation. These findings suggested that the embryonal tissue secretes immunosuppressive factors or enhances inherent suppressive mechanisms in the host. Figures 3; references 14: 12 Russian, 2 Western.

UDC 612.812+612.015.3:551

#### Effects of High Temperature and Humidity on Mental State and Metabolism

907C0244A Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 15 No 4, Jul-Aug 89 (manuscript received 1 Mar 88) pp 92-96

[Article by A. S. Slanazarov, V. P. Makhnovskiy and E. I. Kuzuya, Institute of Alpine Physiology and Experimental Pathology, Kirghiz SSR Academy of Sciences, Frunze]

[Abstract] The effects of a combination of high temperature and humidity on mental state and metabolism were studied in a group of 20 men, 18-20 years old. The studies were conducted in a chamber adjusted to 50°C and a relative humidity of 80 percent, with an average maximum exposure of 20.2 min. Neuropsychologic testing revealed that as a result of such exposure, indicators of logical thinking decreased by 54.6-64 percent, and attentiveness indicators, by an average of 32.1 percent. Concomitantly, metabolic studies demonstrated activation of sympathetic mechanisms: urinary epinephrine rose by 68.9 percent and norepinephrine by 151.4 percent. Other data indicated activation of lipid peroxidation by 55.1 percent and elevation of unconjugated bilirubin in the blood by 54.8 percent. These observations demonstrated that a combination of high temperature and humidity exerts an adverse effect on mental faculties. The latter may be related to elevation of unconjugated bilirubin in the blood which transgresses the blood-brain barrier and may lead to uncoupling of

oxidative phosphorylation in brain mitochondria. Figures 1; references 24: 9 Russian, 15 Western.

UDC 612.17+612.18

### Cardiac, Vascular, and Coronary Components in Cardiovascular Response to Antiorthostasis

907C0704B Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I. M. SECHENOVA  
in Russian Vol 76 No 2, Feb 90 (manuscript received 11 May 89) pp 219-226

[Article by L. I. Osadchiy, T. V. Baluyeva, and I. V. Sergeyev, Laboratory of Circulatory Physiology, Institute of Physiology imeni I. P. Pavlov, USSR Academy of Sciences, Leningrad]

[Abstract] Cardiac, vascular, and coronary components of the cardiovascular response to 15-45° antiorthostasis for 120 sec were analyzed to ascertain individual inputs into the overall response. At inclinations of 15, 30, and 45° most of the animals (61, 58, and 70 percent, respectively) responded with a drop in blood pressure, some (14, 25, and 19 percent) with relatively modest elevation, and a minority with no change. Changes in blood pressure were independent of the angle of inclination, but dependent on baseline blood pressure. With a baseline blood pressure of 134 mm Hg the animals responded with a hypotensive change, and with a baseline of 89 mm Hg they responded with hypertension. The corresponding cardiac output in those two groups was 427 and 433 ml/min, respectively, and the increase in cardiac output in animals with a hypotensive response was unaffected by the angle of inclination. Furthermore, while the angle of antiorthostasis had no effect on the magnitude of hypotensive response, the hypertensive response was directly related to the magnitude of inclination. The incidence of a decrease in coronary blood flow increased with an increase in the magnitude of the angle of inclination, with all animals showing a reduction of approximately 24 percent at 45°. These findings were consistent with a pressure increase of 12 mm Hg on the carotid sinus, with resultant vasodilation. The net effect was a reduction in blood pressure or attenuation of a hypertensive effect in the face of an increase in the cardiac output due to the increase in venous return. Figures 4; references 18: 11 Russian, 7 Western.

UDC 612.117:612.111.11

### Blood Rheology in Rats Following Partial Replacement of Blood Volume With Modified Hemoglobin Solution

907C0704A Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I. M. SECHENOVA  
in Russian Vol 76 No 2, Feb 90 (manuscript received 20 Apr 89) pp 192-199

[Article by V. N. Shuvayeva, N. P. Kuznetsova, and V. A. Levto, Laboratory of Circulatory Physiology, Institute of Physiology imeni I. P. Pavlov, and Laboratory of

Physical Chemistry of Polyelectrolytes and Physiologically Active Polymers, Institute of Macromolecular Compounds, USSR Academy of Sciences, Leningrad]

[Abstract] Male Wistar rats, 270-320 g, were employed in a study designed to assess the rheologic sequelae of replacement of 50-60 percent of the blood volume with a solution of modified hemoglobin (270-320 kD molecular weight; 10.4 percent concentration, 9 percent methemoglobin,  $P_{50} = 13$  mm Hg). Infusion of the replacement solution resulted in a fall of hematocrit from 42-46 percent to 20-25 percent. Adverse effects on blood rheology were apparent immediately and most pronounced within half hour of infusion, and included an increase in the erythrocyte sedimentation rate, blood viscosity, and shear stress. After 3 h moderate improvements were noted, including a reduction in the rate of aggregation and sedimentation of erythrocytes. In general, changes in blood rheology were attributed to the high molecular weight of the modified hemoglobin and its effects on erythrocyte behavior. Figures 1; tables 3; references 9: 8 Russian, 1 Western.

UDC 612.821+612.822.3

### Emotional Stress and Spatial Synchronization of Brain Potentials

907C0701A Moscow ZHURNAL VYSSHEY NERVENOY DEYATELNOSTI IMENI I. P. PAVLOVA  
in Russian Vol 40 No 2, Mar-Apr 90 (manuscript received 24 Jun 88; after revision 17 Feb 89) pp 254-262

[Article by M. N. Rusalova, Institute of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow]

[Abstract] Electroencephalogram patterns were analyzed in 23 healthy right-handed subjects 18-27 years of age, with well-expressed alpha rhythms in order to assess the interrelationship between stress and synchronization of brain potentials. The essential experimental conditions involved imagined anticipation of a painful or neutral stimulus or presentation of a light flash preceding a painful stimulus. The results demonstrated that the highest degree of coherence prevailed in the imagined anticipation of a painful stimulus, followed by imagined anticipation of a neutral stimulus, and then by actual anticipation of a neutral stimulus, and finally actual anticipation of a painful stimulus. The data were interpreted to indicate that emotional factors may either serve to enhance or disorganize spatial synchronization of brain potentials. Spatial synchronization was reinforced in situations in an active situation, but diminished in passive avoidance settings. Figures 5; references 16: 14 Russian, 2 Western.

UDC 612.821.6+612.8.015

**Effects of Prolyl-Leucyl-Glycinamide on  
Behavioral and Visceral Functions in Dogs**

907C0701B Moscow ZHURNAL VYSSHEY  
NERVNOY DEYATELNOSTI IMENI I. P. PAVLOVA  
in Russian Vol 40 No 2, Mar-Apr 90 (manuscript  
received 20 Jan 89; after revision 15 Nov 89) pp 372-373

[Article by V. A. Pastukhov and T. K. Lozhkina, Laboratory of Neuroses, Institute of Physiology imeni I. P. Pavlov, USSR Academy of Sciences, Leningrad]

[Abstract] A series of studies were designed to evaluate the effects of prolyl-leucyl-glycinamide (PLG) on behavioral and visceral functions in dogs. The studies involved intramuscular injections of PLG, as well as administration into the anterior limbic region and dorsal hippocampus under control and stress conditions. The results demonstrated that PLG affects conditioned reflexes and a number of autonomic functions (heart rate, respiratory rate, and motility of gastrointestinal tract). The data were consistent with the view that PLG exerts a stabilizing effect on higher nervous activity in healthy control animals, but seems to be ineffective in neurotic conditions. Tables 1; references 3: 2 Russian, 1 Western.

### Characteristics of the Reproduction of the Turkmen SSR Population

907C0763A Ashkhabad ZDRAVOOKHRANENIYE  
TURKMENISTANA in Russian No 2, Feb 90 pp 3-6

[Article by N. B. Dmitriyeva and Sh. B. Batyrov, All-Union Scientific Research Institute for Hygiene, Economics and the Management of Health Care imeni N. A. Semashko]

[Text] It is now increasingly urgent to have an effective demographic policy which takes into account the development levels of various regions in the country and which is directed towards increasing life expectancy and labor force participation and strengthening the family. Republics in the USSR are in different stages of demographic development. While the Baltic republics, the RSFSR, the Ukraine and Belorussia have modern types of reproduction and population structures, the union republics of Central Asia are at the "starting point." The Turkmen SSR, which has many unsolved problems, has a special place in this regard.

The Turkmen SSR has high birthrates and infant mortality rates and relatively higher general mortality in some age and sex groups than do other republics. All this is reflected in average life expectancy, an indicator of public health. During 1985-1986 average life expectancy in the Turkmen SSR was lower than in all republics. It was 64.8 for the total population (61.4 for men and 67.8 for women).

An analysis of changes in the republic's population shows the uneven growth rates: The greatest increase took place between the censuses of 1959 and 1970, later there was a slowdown in population growth rates. Between 1959 and 1970 the population increased 41.9 percent (46.7 percent in urban areas, 37.8 percent in rural areas); during 1970-1979 it grew 28.4 percent (27.3 and 29.4 percent respectively); and during 1979-1987—21.8 percent (21.3 and 22.3 percent). Between 1959 and 1987 the population of the Turkmen SSR more than doubled (122.1 percent). The growth rate in urban areas (126.0 percent) was greater than in rural areas (118.1 percent).

The republic has a favorable age structure for males and females. This increases birthrates. This must be considered in long term planning of obstetric-gynecological and pediatric services, which should be based upon the predicted birthrates and population size.

The marriage rate is a factor having an important influence upon birthrates. The Turkmen SSR, similar to other republics in Central Asia, has experienced changes in marriage rates, in particular an increase in the age of entering the first marriage.

Data from a selective social-demographic survey conducted in 1985 make it possible to trace, by generation, the dynamics of women's first marriage prior to age 20. Thus, in the generation of 1935-1939, 381 out of every

1,000 women asked said that they had married before they were 20, in the generation of 1940-1944, 480 had; in the generation of 1945-1949—422; 1950-1954—410, 1955-1959—325 and 1960-1964—only 216. A comparative look at these figures for the urban and rural populations shows that early marriages have been significantly reduced, especially among rural women.

Among men the tendency is the opposite—towards marriage at a younger age. Thus, in the generation of 1935-1939, 404 out of 1,000 men asked said they got married before they were 23, in the 1940-1944 generation this figure was 350, 1945-1949—419; 1950-1954—546; and 1955-1959—553 out of 1,000.

Marriage rates have declined significantly for the entire population of the republic. This contrasts to data for the USSR. While in 1959, 710 out of 1,000 men and 637 out of 1,000 women were married, by 1985 the figures were 659 and 588 (the figures for the USSR are 730 and 588).

These changes in marriage rates are not only due to social-economic changes, but also due to changes in the value placed upon marriage, children, etc. National traditions are very important in the republic. All this is reflected in the evolution of the modern family. A relatively low, but growing, divorce rate helps keep the birthrate in the Turkmen SSR relatively high. In 1960 there were 0.5 divorces per 1,000 in the Turkmen SSR, in 1970—1.2; 1980—1.4; and in 1987—1.4. For the USSR these figures were 1.3; 2.6; 3.5 and 3.4. Special coefficients (the number of divorces per 1,000 married couples) show changes in the divorce rate. Thus, for 1958-1959 this coefficient was 2.2 in the republic, in 1969-1970—6.6; in 1978-1979—6.6; and in 1984-1985—8.1.

People in the Turkmen SSR have large families. In 1970 the average family size in the republic was 5.2 (4.6 in urban areas—6.0 in rural areas), by 1979 it had increased to 5.5 people (unchanged in urban areas, but increased to 6.5 in rural areas). These changes were primarily due to increases in the number of families with 9-10 or more members, especially in rural areas. In 1970 7.2 percent of urban families had 9-10 or more members, while in rural areas the figure was 17.0 percent; by 1979 this had increased to 8.7 and 24.3 percent respectively. This increase in very large families is due to the increase in the number of extended families consisting of two or more married couples. This is explained by the retention of the native tradition of having many children and of multi-generation extended families.

A study of the dynamics of general birthrates during 1960-1987 indicates that during this time they have declined 21 percent for the urban population and 4.8 percent for the rural population. It should be noted that while in 1960 the birthrate in rural areas was only 9.4 percent higher than in urban areas, at present it is 32 percent higher.

During 1965-1966 there was a reduction in the special coefficient of birthrates (the ratio of the number of



children born to the number of women of reproductive age, usually 15 to 49 years). This coefficient reached a minimum (16.1) in 1980-1981. Later it increased by 5.8 percent.

At present the republic has stable birthrates for ages up to 20 years and the 20-24 age group, while they have increased for age groups 25-29, 30-34 and all others (See Table 1).

**Dynamics of Birthrate by Age Group during 1958-1987 (per 1,000 women)**

Years	Average Number of Women Giving Birth Per Year								Total Birthrate Coefficient
	Age, Years								
	Under 20	20-24	25-29	30-34	35-39	40-44	45-49	15-49	
1958-1959	39.5	216.2	251.2	217.2	173.4	93.1	34.0	161.6	5026
1965-1966	32.7	282.6	290.9	251.2	200.1	109.9	40.3	176.6	6023
1969-1970	33.5	271.1	276.2	250.5	213.0	110.2	31.4	165.6	5972
1975-1976	23.4	265.5	292.5	243.3	181.0	103.6	23.5	155.6	5738
1978-1979	21.8	256.2	289.3	229.6	151.2	88.1	18.3	151.3	5277
1980-1981	21.6	246.5	273.9	204.0	151.9	71.1	15.0	148.2	4930
1982-1983	21.4	243.9	281.8	196.7	137.6	58.4	11.1	149.6	4741
1984-1985	20.1	238.4	293.7	196.7	125.5	50.0	8.7	151.2	4664
1985-1986	20.4	240.6	303.7	199.6	121.8	51.2	7.7	154.5	4718
1986-1987	20.7	239.0	311.0	204.8	119.6	51.9	7.1	156.8	4752

One consequence of the unique dynamics of the birthrate indicator is a change in the total coefficient of the birthrate characterizing the average number of births per woman in a hypothetical generation throughout her entire life while the present birthrate levels for each age are retained. An increase in special coefficients of birthrates has also been accompanied by an increase in total coefficients with a small time lag. These increased from 4.664 in 1984-1985 to 4.752 in 1986-1987. It should be noted that in spite of their fluctuations, the size of these total coefficients is evidence of the population's expanded reproduction.

The change in the birthrate indicator for various age groups has led to a change in the birthrate structure with regard to the number of births per family. It is known that the share of first births and that of fourth and subsequent births is an indicator of the birthrate—the higher the birthrate the lower the share of first births. During 1980-1986 there was a sizable change in the birthrate structure. In urban areas in the republic families with 1-4 children accounted for 77.8 percent of the total. By 1986 this had increased to 83.8 percent. For rural areas the figures were 66.4 and 73.5 percent respectively.

These data indicate that the republic is showing a tendency characteristic for more progressive types of birthrates, i.e. the concentration of births at a younger age. However, in rural areas this process will be considerably slower than in urban. To a considerable degree this is due to the traditional forms of family and marriage relationships among the native population. Public opinion is very important here.

A tendency for birthrates to decline is an objective process and a historic transition to mass intrafamily regulation of the birthrate, the beginning stage of which is characteristic for the present level of the Turkmen people's demographic development. One of the tasks for regional demographic policies should now be the implementation of measures to prevent undesirable consequences of this tendency, that is, to stop the possibility of families with 1-2 children becoming the predominant type of family, similar to other regions. It is very important to educate the population about demographics and to give people values appropriate to the goals of demographic policy. This should be implemented through extensive propaganda concerning birthrates, family planning, the strengthening of the family, and through reductions in mortality and increases in life expectancy.

UDC 616-084.3(47+57)

#### **Effect of Dispensarization on Some Public Health Indicators and Work of Medical Institutions**

907C0697A Moscow SOVETSKOYE  
ZDRAVOOKHRANENIYE in Russian No 1 Jan 90  
pp 33-37

[Article by V. A. Minyayev, L. A. Alekseyeva and L. A. Zavyalova; 1st Leningrad Medical Institute imeni I. P. Pavlov]

[Abstract] "Basic trends of development of health protection of the people and reconstruction of USSR public health care in the 12th Five-Year Plan and up to 2000" states that continuous dynamic observation of Soviet

citizens throughout their life is of paramount importance. Execution of this strategy requires consideration of changing needs of the people for different forms of medical assistance. Results of an experiment on universal dispensarization performed at Leningrad polyclinic NO. 31 under direction of the chair of social hygiene and public health organization 1st Leningrad Medical Institute imeni I. P. Pavlov provided much data for carrying out the strategy. This article described the state of medical assistance and presented indicators of medical work for 1985 at experimental sections divided into smaller units and including nearly 1000 adult inhabitants. Work on general dispensarization has been underway for 7 years at these sections and at control sections of identical composition with 1700 inhabitants. The study revealed many more patients of identical age-sex composition in the experimental sections after introduction of general dispensarization than in control sections (70.4 percent as compared to 55.8 percent) and detection of more diseases. General dispensarization produced a significant increase in disease detection, visits to physicians, improvement in diagnosis and curative measures and health improvement measures. Long-term active general dispensarization greatly decreased the frequency of severe forms of diseases, complications and aggravations of chronic diseases. It produced improved economic and social effects by saving hospital beds and time and saving labor resources. The overall dispensarization at territorial sections divided into smaller units increased the effectiveness of territorial polyclinics and district physicians.

UDC 616-007-053.1-084

### Problem Concerning Prevalence of Congenital Defects of Development

907C0697B Moscow SOVETSKOYE  
ZDRAVOOKHRANENIYE in Russian No 1, Jan 90  
pp 41-43

[Article by B. Ya. Reznik and I. P. Minkov; Odessa Medical Institute imeni N. I. Pirogov]

[Abstract] Studies of the history of births and charts of 42,275 neonates, individual charts of development of 38,280 children from the 1st day after release from nursing homes (6 days) up to the age of 15 years and history of diseases and autopsy material from 4153 children ranging in age from birth to 15 years, observed and treated in a clinic, were performed from 1979-1987. Congenital developmental defects in the children from birth to the age of 15 years was 2.83 percent. This indicator was somewhat higher in the last 3 years in comparison with 1979-1981 (3.27 percent to 2.16 percent). Among the stillborn, congenital defects occurred in 10.2 percent of the children. Congenital defects among neonates equalled 13.8 per 1000. While the incidence in 1979-1981 was 7.1 percent, it was 18.2 percent in 1985-1987 and 22.4 percent in 1987 alone.

Major anomalies were listed and discussed. Malformations of the central nervous system and malformations of the gastrointestinal tract or cardiovascular system made up most of the defects. Methods of congenital defect preventions were presented and groups at high risk were identified. References 7: 6 Russian; 1 Western.

UDC 614.2:658.52.011.56

### Some Problems of Development of Public Health Automatic Control System

907C0698A Moscow ZDRAVOOKHRANENIYE  
ROSSIYSKOY FEDERATSII in Russian No 1, Jan 90  
pp 31-34

[Article by G. I. Chechenin; Novokuznetsk Group Medical Information-Computer Center of Municipal Health Department, Medical Cybernetics and Informatics, Novokuznetsk Institute for Advanced Training of Physicians]

[Abstract] An article "Problems of Creating an Automatic Control System in Public Health Care" by Yu. M. Komarov, published in ZDRAVOOKHRANENIYE ROSSIYSKOY FEDERATSII No. 5, 1988, was discussed and criticized. Komarov pointed out deficiencies and errors in the attempt to improve public health control based on use of computer technology and an automatic control system. Komarov's analysis of deficiencies included presentation of means for overcoming these errors and means of reconstructing the entire operation for creating an automatic control system in public health care. Some of Komarov's conclusions and positions were disputed in this article. This article emphasized the unsuitableness of the public health system to operate under an automatic control system because of incorrect posing of questions concerning this matter due to the absence of methodical materials and trained personnel. 20 years of study have not produced a final version of methodical recommendations for development of a public health automatic control system. Means for improving the system were described and discussed. The importance of retaining competent personnel at public health computer centers and replacing obsolete computer equipment was emphasized. References 15 (Russian).

### Performance of 'Family Physician' Experiment in Outpatient-Polyclinic Institutions of Kazakh SSR

907C0698B Moscow ZDRAVOOKHRANENIYE  
KAZAKHSTANA in Russian No 1, Jan 90 pp 9-12

[Article by G. G. Urmurzina, G. A. Zhetpisbayeva, N. F. Ilicheva and N. A. Belimova; Kazakh SSR Ministry of Health, Alma-Ata Institute For Advanced Training of Physicians, USSR Ministry of Health]

[Abstract] An experiment involving introduction of a new form of organization of work of the primary (family) physician, begun in Kazakhstan in September 1989, is

aimed at elimination of inadequacies in the previous system and complete satisfaction of the population's medical needs, especially the need for outpatient polyclinic assistance, improvement of quality of medical care, reduction of the number of unnecessary consultations and laboratory studies. Preparatory and organizational work involving a wide range of Kazakh Ministry of Health specialists and educational institutions with participation of public health agency directors, scientists and teachers of the Alma-Ata Institute for the Advanced Training of Physicians, USSR Ministry of Health preceded the experiment. At the 1st stage of the experiment, provision of training to the family physician by a number of therapists and, later, by pediatricians and then by rural physicians of many specialties permitted correction of the program as needed. The trained family physicians will work with 2 nurses and will provide care

for 300-350 families (1000-1200 persons). The payment system was described. The training program lasted for 2 months. Pediatric training (including neonatology) made up 28 percent of the training time; therapy training made up more than 10 percent of the training time. Organization of labor, legislation, fitness for work expertise, health evaluation and collaboration with other specialists made up nearly 20 percent of the training time. Nearly 9 percent of the training time was devoted to care of infectious diseases. Training time was given to other areas of medicine and the training program was corrected as needed. Women made up 91 percent of the trainees. Results of the training program will be available in the 1st quarter of 1992 and they will permit objective evaluation of the new form of primary medical and sanitation assistance.

UDC 577.391;611.8.591.48

**Morphometric Analysis of Early Neuronal Reaction to Superhigh Dose of Radiation***907C0159 Ama-Ata VESTNIK AKADEMII NAUK KAZAKHSKOY SSR in Russian No 9, Sep 89 pp 50-54*

[Article by A. A. Abdrakhmanov, A. R. Rakhishev and A. V. Karamysheva]

[Abstract] An analysis was conducted on the early ultrastructural changes in the sensorimotor cortex of outbred male rats (180-210 g) subjected to 150 Gy (25-30 Gy/min) gamma-irradiation. The immediate changes included a statistically significant increase in the percentage of hypochromic neurons in layers IV and V and extensive chromatolysis. During the first 6 h, mitochondrial swelling and vacuolization was also in evidence, while the endoplasmic reticulum underwent fragmentation and irregular dilatation. After 24 h, the ultrastructure of the hypochromic neurons remained unaltered. In addition, an increase in the density of the mitochondrial matrix became evident 15 min after irradiation, while the density of the Golgi apparatus remained unaltered and that of the endoplasmic reticulum decreased. After 6 h, the density of the mitochondria and the lysosomes increased appreciably. After 24 h, the densities of these organelles diminished in comparison with the early changes. In general, on an overall basis the data also showed that the hyperchromic cells were observed to be even more labile than the hypochromic neurons. However, the sensorimotor neurons evidently possess sufficient functional reserves to withstand more severe destruction from supralethal doses of gamma-radiation. Figures 1; references 7 (Russian).

UDC 577.391.621.386.86

**Pharmacodynamics in Irradiated Rats***907C0243A Moscow RADIOBIOLOGIYA in Russian Vol 29 No 4, Jul-Aug 89 (manuscript received 16 Dec 87) pp 492-494*

[Article by Z. Z. Khakimov, Central Scientific Research Laboratory, Tashkent State Medical Institute]

[Abstract] A comparative evaluation was conducted on the pharmacodynamics of hexenal (100 mg/kg, i.p.), meprobamate (150 mg/kg, i.p.), ethylmorphine (20 mg/kg, i.p.), and amidopyrine (30 mg/kg, i.p.) administered

to male albino rats (180-200 g) 3 and 6 days after whole-body 8 Gy  $\gamma$ -irradiation. The results demonstrated that pharmacodynamics in the 3-day series did not differ from the pharmacodynamics observed in unirradiated control rats. However, administration after 6 days resulted in statistically significant prolongation and intensification of the drug effects. Concomitant metabolic studies showed significant depression of hepatic amidopyrine demethylase, aniline hydroxylase, and NADPH-cytochrome C-reductase activities, as well as diminished concentrations of microsomal proteins and cytochromes P-450 and  $b_5$ . These observations demonstrated that the process of radiation sickness potentiates pharmacodynamics due to impaired detoxication mechanisms in the animal model, suggesting the need for careful drug monitoring in patients with radiation injuries. References 22 (Russian).

UDC 577.391.634.948

**Cysteamine Protection of Plants from Chronic and Acute  $\gamma$ -Irradiation Damage***907C0243B Moscow RADIOBIOLOGIYA in Russian Vol 29 No 4, Jul-Aug 89 (manuscript received 10 Oct 88) pp 501-505*

[Article by I. N. Gudkov, K. A. Giginayshvili and D. M. Grodzinskiy, Ukrainian Agricultural Academy, Kiev; Tbilisi State University; Institute of Botany imeni N. G. Kholodnogo, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] Ramonskiy 77 peas were used in determining the relative efficacy of cysteamine, in terms of the dose modification factor (DMF), in chronic and acute radiation exposure. In the chronic studies the plants were grown for 71 days in conjunction with 18 h/day  $\gamma$ -irradiation to cumulative doses of 7.1-56.8 Gy (0.1-0.8 Gy/day); twice a week the plants were sprayed with 0.01 M aqueous cysteamine solution. Acute studies involved irradiation of 10-, 20-, 35-, and 45-day-old plants with 5-14 Gy  $\gamma$ -irradiation; 3, 1 and 0.5 h before irradiation the plants were sprayed with the cysteamine solution. Analysis of the data revealed that in the chronic experiments the DMF was 1.15, and in the acute series 1.4-2. The diminished efficacy in the chronic experiment was attributed to efficient repair systems. Accordingly, search for radioprotective agents in situations of long-term irradiation should concentrate on agents that enhance normal repair mechanisms. Figures 2; references 4 (Russian).



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**Therapeutic Efficacy of Alcoholic Plasma Extract  
in Combined Ionizing Radiation-Thermal Injury**

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Vol 29 No 4, Jul-Aug 89 (manuscript received  
24 Oct 88) pp 524-528

[Article by V. Ye. Ryabinin, A. L. Tsytovich, L. F. Charnaya, R. I. Lifshits, A. N. Kharisov and V. S. Potapov, Chelyabinsk Medical Institute]

[Abstract] An alcoholic extract of donor plasma was tested for its therapeutic benefits in outbred and (CBA x C57Bl)F<sub>1</sub> mice with combined ionizing radiation-thermal injuries. The animals were subjected to 3.4 Gy irradiation from a Cs-137 source and within 15-20 min with third-degree burn over 8-10 percent of the body surface from a halogen lamp. One hour after the last insult, the animals were treated intravenously with 14-17 mg/kg of the extract peptide preparation. Multifaceted assessment showed the alcoholic extract to have considerable therapeutic promise. The mortality for outbred control rats was 20 percent in 1 h, 60 percent in one day, and 100 percent in 8 days. The corresponding figures for plasma extract-treated animals were 0 percent, 43 percent and 85 percent. In addition, the extract promoted recovery of psychomotor activity, enhanced oxygen uptake, and promoted wound healing. Administration of the extract also attenuated the extent of lipid peroxidation in the brain and liver of injured mice, while in vitro studies showed the extract to diminish chemiluminescence of control and latex particle-activated neutrophils by 65 percent and 85 percent. These findings suggest that

extract of this type should be considered for more extensive therapeutic studies. References 9: 5 Russian, 4 Western.

UDC 577.391.538.56.612.273

**Possible Mechanisms of Radiomodifying Effects  
of Exogenous Hypoxia and UHF Electromagnetic  
Radiation**

907C0243D Moscow RADIOBIOLOGIYA in Russian  
Vol 29 No 4, Jul-Aug 89 (manuscript received  
27 May 88) pp 529-532

[Article by R. I. Tabukashvili and I. B. Ushakov, Tbilisia State Medical Institute]

[Abstract] Male rats, 200-220 g, were employed in studies designed to further assess the influence of various exogenous factors on radiotolerance—in this case, hypoxia and UHF irradiation. The results were interpreted in terms of 30-day survival statistics after 8.5 Gy (79.3 Gy/min)  $\gamma$ -irradiation. The mortality rate for untreated control animals was 100 percent. Animals subjected to hypoxia (5 percent O<sub>2</sub>) for 8 min followed by  $\gamma$ -irradiation had a survival rate of 27 percent, while animals pretreated with liver extract from hypoxia-exposed animals and  $\gamma$ -irradiated 15 min later had a survival rate of 10 percent. Finally, a 20 percent survival rate was obtained with rats treated with liver extract from animals exposed to UHF irradiation (2.45 GHz, 100 mW/cm<sup>2</sup>, 8 min) and  $\gamma$ -irradiated 15 min later. These findings indicate that exposure to environmental stress factors, such as hypoxia and UHF radiation, leads to production of bioactive substances that alter metabolic mechanisms in the direction of enhanced radioreistance. References 15: 14 Russian, 1 Western.

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